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

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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF Extract of *Sorghum bicolour* leaf, *Pterocarpus osun* stem, *Piper guineense* seed and *Caryophylli* flower for the treatment of sickle cell disease

On 26 August 2005, orphan designation (EU/3/05/302) was granted by the European Commission to Xechem UK Ltd., United Kingdom, for extract of *Sorghum bicolour* leaf, *Pterocarpus osun* stem, *Piper guineense* seed and *Caryophylli* flower for the treatment of sickle cell disease.

What is sickle cell disease?
Sickle cell disease is a group of inherited diseases caused by a mutation in a blood protein called haemoglobin, leading to a so-called "hemoglobin S". 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 disease can be remarkably variable. Some patients remain without much of complaints, while others suffer repeated crises requiring admission to hospital from early childhood.

What are the methods of treatment available?
No medicines exist that have been authorised for the treatment of sickle cell disease. 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*?
According to the information provided by the sponsor, sickle cell disease was considered to affect less than 78,000 persons in the European Union.

How is this medicinal product expected to act?
Red blood cell sickling involves the polymerisation (molecules joining together into a chain) of hemoglobin S. Extract of *Sorghum bicolour* leaf, *Pterocarpus osun* stem, *Piper guineense* seed and *Caryophylli* flower was shown to block (inhibit) the polymerisation of this hemoglobin S and might therefore reduce the number of sickle cells in the blood. This might help to reduce the severity of the disease.

What is the stage of development of this medicinal product?
At the time of submission of the application for orphan designation, clinical trials in patients with sickle cell disease were ongoing.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.eu.int www.emea.eu.int

Extract of *Sorghum bicolour* leaf, *Pterocarpus osun* stem, *Piper guineense* seed and *Caryophylli* flower was not marketed anywhere worldwide for treatment of sickle cell disease, at the time of submission. Orphan designation of the medicinal product (as "Niprisan") was granted in USA for treatment of sickle cell disease.

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

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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.

For more information:
Sponsor's contact details:
Xechem UK Ltd
The White House
2 Meadrow
Godalming
Surrey GU7 3HN
United Kingdom
Telephone: +44 20 86 41 30 35
Telefax: +44 87 04 28 25 52
E-mail: martin.biggs@mba-gbm.com

Patients' associations contact points :

Sickle Cell Society
54 Station Road
London
NW10 4UA
United Kingdom
Telephone: +44 (0) 20 8961 7795
Telefax : +44 (0) 20 8961 8346
E-mail: info@sicklecellsociety.org

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

APIPD : Association pour l'Information et la Prévention de la Drépanocytose
7 ter Rue Edouard Vaillant
93400 Saint-Ouen
France
Telephone :+33 1 40 10 02 49
Telefax : +33 1 40 10 96 38
E-mail: jenny.hippocrate@free.fr

Associazione Talassemici e Drepanocitici Lombardi (A.T.D.L)
c/o A.V.I.S. Comunale
L.go Volontari del Sangue, 1
20133 Milano
Italy
Telephone: +39 02 70 63 87 96
Telefax: +39 1 78 22 89 515
E-mail: info@atdl.it

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

Language	Active Ingredient	Indication
English	Extract of *Sorghum bicolour* leaf, *Pterocarpus osun* stem, *Piper guineense* seed and *Caryophylli* flower	Treatment of sickle cell disease
Czech	Extrakt z listů *Sorghum bicolour*, stvolů *Pterocarpus osun*, semen *Piper guineense* a květů lístků *Caryophylli*	Léčba srpkovité anémie
Danish	Extrakt of *Sorghum bicolour* blade, *Pterocarpus osun* stængel, *Piper guineense* frø og *Caryophylli* blomster	Behandling af seglcellesygdom
Dutch	Extract van *Sorghum bicolour* blad, *Pterocarpus osun* stam, *Piper guineense* zaad en *Caryophylli* bloem	Behandeling van sikkelcelaandoening
Estonian	*Sorghum bicolour* lehe, *Pterocarpus osun* varre, *Piper guineense* seemne ja *Caryophylli* õie ekstrakt	Sirprakulise aneemia ravi
Finnish	Ekstrakti, joka sisältää *Sorghum bicolour* lehteä, *Pterocarpus osun* vartta, *Piper guineense* siementä ja *Caryophylli* kukkaa	Sirppisolusyndrooman hoito
French	Extrait de feuille de *Sorghum bicolour*, de tige de *Pterocarpus osun*, de graine de *Piper guineense* et de fleur de *Caryophylli*	Traitement du syndrome drépanocytaire
German	Extrakt des *Sorghum bicolour* Blatts, des *Pterocarpus osun* Stamms, des *Piper guineense* Samens and der *Caryophylli* Blüte	Behandlung der Sichelzellenanämie
Greek	Εκχύλισμα φύλλων *Sorghum bicolour*, μίσχου *Pterocarpus osun*, σπόρου *Piper guineense* και άνθους *Caryophylli*	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	*Sorghum bicolour* folium, *Pterocarpus osun* herba, *Piper guineense* semen és *Caryophylli* flos kivonat	Sarlósejtes anaemia kezelése
Italian	Estratto di foglia di *Sorghum bicolor*, fusto di *Pterocarpus osun*, seme di *Piper guineense*, e fiore di *Caryophylli*	Trattamento dell'anemia falciforme

Latvian	*Sorghum bicolour* lapu, *Pterocarpus osun* stumbra, *Piper guineense* sēklu un *Caryophylli* ziedu ekstrakts	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	*Sorghum bicolour* lapų, *Pterocarpus osun* stiebų, *Piper guineense* sėklų ir *Caryophylli* žiedų ekstraktas	Siklemijos gydymas
Polish	Wyciąg z liścia *Sorginum bicolour*, łodygi *Pterocarpus osum*, nasion *Piper guinese* i kwiatu *Cryophyli*	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Extracto da folha de *Sorghum bicolour*, caule de *Pterocarpus osun*, semente de *Piper guineense* e da flor de *Caryophylli*	Tratmento do sindrome das células falciformes
Slovak	Extrakt z listov *Sorghum bicolor*, zo stonky *Pterocarpus osun*, zo semien *Piper guineense* a kvetov *Caryopphylli*	Liečba kosáčikovej anémie
Slovenian	Izvleček lista *Sorghum bicolour*, stebla *Pterocarpus osun*, semena *Piper guineense* in rože *Caryophylli*	Zdravljenje bolezni srpastih celic
Spanish	Extracto de hoja de *Sorghum bicolour*, tallo de *Pterocarpus osun*, semilla de *Piper guineense* y flor de *Caryophylli*	Tratamiento de la anemia drepanocítica
Swedish	Extrakt från *Sorghum bicolor* blad, *Pterocarpus osun* stam, *Piper guineense frö*, *Caryophylli* blomma	Behandling av sickle cell syndrom
Norwegian	Ekstrakt av *Sorghum bicolour* blad, *Pterocarpus osum* stilk, *Piper guineense* frø og *Carophylli* blomst	Behandling av sigdcellesykdom
Icelandic	Extrakt af *Sorghum bicolour* blöðum, *Pterocarpus osun* stilkum, *Piper guineense* fræjum og *Caryophylli* blómum	Meðferð sigðkornablóðleysis