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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Dihydroartemisin, piperaquine for the treatment of malaria

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in July 2011 on request of the sponsor.

On 3 August 2007, orphan designation (EU/3/07/468) was granted by the European Commission to Sigma Tau Industrie Farmaceutiche Riunite S.p.A, Italy, for dihydroartemisinin, piperaquine for the treatment of malaria.

What is malaria?

Malaria is an infectious disease caused by *Plasmodium* parasites. There are four species of *Plasmodium* that may infect humans: *P. vivax*, *P. malariae*, *P. ovale* and *P. falciparum*. Malaria is carried from person to person by *Anopheles* mosquitoes, and transmission occurs mostly in tropical and subtropical regions including parts of the Americas, Asia, and Africa. In Europe, malaria is mainly encountered in travellers returning from these areas. Following a bite from an infected mosquito, the parasite goes to the liver. When the parasite then enters the bloodstream it infects and destroys red blood cells.

Fever is the major symptom of malaria. In addition, flu-like symptoms such as chills, headaches, muscle-aches, and fatigue can occur. Malaria due to *P. falciparum* may progress rapidly causing seizures, coma, breathing and kidney problems. The disease is life-threatening, and active malaria infection with *P. falciparum* is a medical emergency requiring hospitalization.

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

At the time of designation, malaria was considered to affect approximately 0.3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 15,000 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 based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

What treatments are available?

Several medicinal products with anti-malarial activity were authorised for the condition in the Community at the time of submission of the application for orphan drug designation.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that the combination of dihydroartemisinin and piperaquine might be of potential significant benefit for the treatment of malaria, mainly because it might improve survival in those suffering severe, life-threatening malaria. The assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Dihydroartemisinin is the active form of artesunate, a chemically modified derivative of the natural product artemisinin, which is found in sweet wormwood. It is proposed that it acts by damaging the membrane of the parasite, thus killing the parasite.

Piperaquine is a chemical compound related to chloroquine, a product extensively used in the treatment of malaria. Its mechanism of action is based on the inhibition of the detoxification by the *Plasmodium* of heme molecules that accumulate in the parasite.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, clinical trials in patients with malaria were ongoing.

Dihydroartemisinin, piperaquine was not authorised anywhere worldwide for malaria, at the time of submission. Orphan designation of dihydroartemisinin, piperaquine was granted in the United States for malaria.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 25 June 2007 recommending the granting of this designation.

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:

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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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Dihydroartemisinin, piperazine	Treatment of malaria
Bulgarian	Дихидроартемизинин, пипераквин	Лечение на малария
Czech	Dihydroartemisinin, piperazin	Léčba malárie
Danish	Dihydroartemisinin, piperazin	Behandling af malaria
Dutch	Dihydroartemisinine, piperazine	Behandeling van malaria
Estonian	Dihydroartemisiiniin, piperakiin	Malaaria ravi
Finnish	Dihydroartemisiiniini, piperakiini	Malarian hoito
French	Dihydroartémisinine, pipérazine	Traitement du paludisme
German	Dihydroartemisinin, Piperazin	Behandlung der Malaria
Greek	Διυδρο-αρτεμισινίνη, Πιπερακίνη	Θεραπεία της ελονοσίας
Hungarian	Dihidro-artemisinin, piperakin (piperazine)	Malária kezelése
Italian	Diidroartemisinina, piperachina	Trattamento della malaria
Latvian	Dihidroartemiziniņš, piperakvīns	Malārijas ārstēšana
Lithuanian	Dihidroartemizininas, piperakvinas	Maliarijos gydymas
Maltese	Dihydroartemisinin, piperazine	Kura tal-malarja
Polish	Dihydroartemizyna, piperachina	Leczenie malarii
Portuguese	Dihidroartemisinina, piperazina	Tratamento da malária
Romanian	Dihidroartemisinin, piperachină	Tratamentul malariei
Slovak	Dihydroartemizinín, piperachin	Liečba malária
Slovenian	Dihidroartemisinin, piperakin	Zdravljenje malarije
Spanish	Dihidroartemisinina, piperazina	Tratamiento del paludismo
Swedish	Dihydroartemisinin, dihydroartemisinin, piperakin	Behandling av malaria
Norwegian	Dihydroartemisinin, piperakin	Behandling av malaria
Icelandic	Tvíhýdróartemísínín, píperakín	Til meðferðar á malaríu

¹ At the time of designation