PRESS RELEASE

Eurartesim® (dihydroartemisinin-piperaquine)

ACT to combat malaria receives marketing authorization from EMA

- A fixed-dose combination therapy to combat malaria, Eurartesim®, (dihydroartemisinin-piperaquine) the product of Italian research conducted by Sigma-Tau and MMV, approved by the European Medicines Agency (EMA)
- Therapy with a simple dosage regimen, up to 3 tablets once a day for 3 days. Studies have demonstrated high cure rates, above 95%, and a significant reduction of re-infection rates compared to leading antimalarial treatments
- Every year almost 250 million people all over the world are affected by malaria. The disease takes the lives of over 780,000 people, mainly in sub-Saharan Africa, 85% of whom are children under 5

Geneva, 30 November 2011. For the very first time, the European Medicines Agency (EMA), using a centralised procedure, has granted regulatory approval to an artemisinin combination therapy (ACT) for the treatment of uncomplicated \textit{P. falciparum} malaria. This ACT, Eurartesim® (dihydroartemisinin-piperaquine), was developed collaboratively by Sigma-Tau s.p.a Industrie Farmaceutiche Riunite, Italy, and the not-for-profit product development partnership Medicines for Malaria Venture (MMV). The development of \textit{Eurartesim} has made Sigma-Tau the first Italian company to be granted marketing authorization for an antimalarial drug by the 27 EU Member States from the EMA.

\textit{Eurartesim}, a fixed-dose combination of two antimalarials, dihydroartemisinin and piperaquine (DHA-PQP), is generally well-tolerated and is administered once a day for 3 days instead of twice a day, making the drug more patient friendly. In addition, clinical trials have shown that compared to other approved ACTs, \textit{Eurartesim} provides better and longer protection from new malaria infections. This is good news for children in high transmission areas who often succumb to another life-threatening malaria episode after they have recovered from the first\textsuperscript{1}.

The EMA’s authorization is based on the results of a series of large-scale clinical trials that assessed \textit{Eurartesim}’s safety and efficacy in comparison to artemether-lumefantrine or artesunate + mefloquine. The studies tested this ACT in more than 2,700 patients in Africa (Burkina Faso, Zambia, Kenya, Mozambique and Uganda) and in Asia (Thailand, India and Laos), in around 1,036 African children aged 6 months to 10 years, all affected by uncomplicated \textit{P. falciparum} malaria.

"Clinical studies carried out on patients treated with \textit{Eurartesim} have confirmed high cure rates, above 95% - says Marco Corsi, Sigma-Tau's Medical Director. Moreover, compared to comparator drugs, \textit{Eurartesim} has shown a secondary protective effect - an almost 50% reduction in the number of new infections in the 2 months following treatment. In highly endemic countries, where treated patients often become newly infected, this secondary protective effect might have a positive outcome on public health. The marketing authorization for Europe will allow us not only to provide a highly effective treatment to vulnerable populations of endemic countries, where malaria has a devastating impact on health and socio-economic systems, but also to European citizens."

Developed to high internationally recognized standards, Eurartesim meets the therapeutic guidelines outlined by the World Health Organization (WHO) which, on the basis of clinical evidence, recommends the combination of two active ingredients in the same tablet: an artemisinin derivative with a high antimalarial efficacy (dihydroartemisinin) and a second antimalarial drug (piperaquine), which helps protect the artemisinin component from the risk of resistance.

“The approval of Eurartesim by the EMA comes at a critical time in the fight against malaria - says David Reddy, CEO, MMV. This high quality treatment is a much-awaited addition to the malaria arsenal and will be welcomed by health care professionals in a number of malaria-endemic countries. Eurartesim is the product of a close collaboration between MMV and Sigma-Tau. The partnership between Sigma-Tau and MMV will continue as we focus on the development of a paediatric formulation of the treatment targeted at children under 5 years of age.”

Malaria burden on mankind

Malaria is one of the most devastating diseases in the world with approximately 250 million new cases reported every year. Of the 780,000 people who die annually from malaria, over 90% are from sub-Saharan Africa, and 85% are children under 5.

On the other hand, most cases of “imported” malaria are reported in Western Europe. Every year there are 10,000 to 12,000 new cases within the EU. According to data from the World Health Organization (WHO), in some areas of Western Europe, and more precisely in France, the United Kingdom, Germany, Italy and Spain from 2000 and 2010 there have been approximately 93,000 malaria cases, the majority of which were caused by P. falciparum which is the most deadly species among the five that cause malaria.

In particular, over the last decade, France is the country most affected by malaria with 56,638 cases, followed by the United Kingdom with 19,132 cases, Germany with 7,581 cases, Italy with 5,881 cases (data available only up to 2007) and Spain with 3,755 cases².

According to data released in recent years the malaria epidemic is continuing to expand worldwide also as a result of climate change which is leading to the expansion of areas where the vector mosquitoes can live and infect people. Over 40% of the world’s population is at risk of infection and, although over 90% of cases occur in Africa, the new frontier of the disease is South East Asia where 83% of the population (over 1.3 billion people) is at risk. According to the World Health Organization, together with HIV/AIDS and tuberculosis, malaria is one of the 3 most widespread diseases in Africa and the leading cause of death in children under 5 year old (the disease is estimated to kill a young child every 30 seconds).

In Europe, autochthonous cases are rare. These are largely cases of people accidentally bitten by infective mosquitoes carried by air carriers. Much larger is the number of cases of imported malaria, i.e. of travellers or migrants infected in countries where malaria is endemic. In 2002, the World Health Organization reported about 230,000 cases of malaria imported into the EU in the past 30 years. In 2007 more than 8,000 cases occurred in the EU.

Notes for editors

About the combination dihydroartemisinin-piperaquine (DHA-PQP)

Dihydroartemisinin (DHA) is obtained from artemisinin, an active ingredient extracted from Artemisia annua (sweet wormwood) a herb used in Chinese traditional medicine for treating “fevers”, which acts very rapidly against the malaria parasite and is rapidly eliminated from the body. Piperaquine (PQP), is a molecule with a much longer half-life than other currently available antimalarials. It stays longer in the body and ensures the

² World Health Organization (http://data.euro.who.int/CISID/).
complete eradication of any residual infection. As a combination, the dosage of DHA-PQP varies by patient weight – children are usually prescribed one tablet a day for 3 days while adults are recommended three tablets once a day for three days.

About Sigma-Tau
Sigma-Tau Group is one of the leading players in the international pharmaceutical industry, and is 100% Italian-owned. The company has always been committed to the research, development and marketing of innovative medicines, in order to improve patients’ well-being and quality of life. Sigma-Tau Group has its headquarter in Pomezia (Rome) and subsidiaries in France, Switzerland, Belgium, Holland, Portugal, Germany, United Kingdom, India, as well as United States and Spain - where the Group owns two production facilities – it has more than 2,400 employees and an expanding network of licensees worldwide. Sigma-Tau was founded in Italy in 1957 and in 2010 hit a turnover of 673 million euros. The company invests 16% of its annual turnover on research and development. Sigma-Tau’s R&D team of 400 people is currently working on 45 projects, from pre-clinical studies to clinical development. Thirty-five studies underwent clinical trials with 26 different molecules, 18 of which mostly (11) new and original, resulting from Sigma-Tau’s research or upon which Sigma-Tau has exclusive rights. The Company’s research and development projects focuses on several therapeautic areas, including rare and neglected diseases that cause a significant social impact, e.g., oncology, immunology and biotech; also, the company’s experience and know-how in cardiovascular diseases, nervous system and metabolic diseases cannot be disregarded.
Sigma-Tau’s website: www.sigma-tau.it

Sigma-Tau’s Malaria Programs
For several years now Sigma-Tau has focused on areas that have a major social and healthcare impact, namely the research and development of drugs for the treatment of rare diseases and malaria. In the case of malaria, the company’s commitment has been made concrete via its partnership with Medicines for Malaria Venture.

About Medicines for Malaria Venture (MMV)
MMV is a leading product development partnership (PDP) in the field of anti-malarial drug research and development. It was established as a foundation in 1999, and registered in Switzerland. MMV’s mission is to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective and affordable anti-malaria drugs. Its vision is a world in which these innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and help to ultimately eradicate this terrible disease.
MMV is currently managing the largest-ever portfolio of over 50 promising antimalarial projects. Its strength comes from its product development partnership (PDP) model reflected in its network of more than 140 pharmaceutical, academic and endemic-country partners in 45 countries. MMV also works in close partnership with Roll Back Malaria (RBM) and a number of WHO programmes that include TDR, the Global Malaria Programme (GMP) and the Essential Medicines Programme. For more information, please visit http://www.mmv.org

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