PRESS RELEASE

Pyramax®, a new antimalarial combination, receives positive opinion from European Medicines Agency

Geneva, 20 February 2012: Pyramax®, a fixed-dose combination of pyronaridine and artesunate, becomes the first antimalarial to be granted a positive scientific opinion from the European Medicines Agency (EMA) under Article 58. This once daily, 3-day treatment is indicated for acute, uncomplicated Plasmodium falciparum and blood-stage Plasmodium vivax malaria in adults and children over 20 kg.

Pyramax tablets are the result of collaboration between the product development partnership Medicines for Malaria Venture, and Shin Poong Pharmaceutical Co. Ltd., Republic of Korea. The approval is based upon clinical trials comparing the safety and efficacy of Pyramax to that of artemether-lumefantrine and a loose combination of artesunate and mefloquine for P. falciparum malaria, and versus chloroquine for P. vivax malaria.

It is the first artemisinin combination therapy (ACT) to be approved by a stringent regulatory authority for the treatment of both P. falciparum and P. vivax malaria, and the only ACT with trials in P. vivax malaria conducted to stringent regulatory standards.

“EMA’s positive scientific opinion of Pyramax comes at a critical time,” said David Reddy, CEO of MMV. “Parasite resistance to artemisinin, as well as to the partner drugs in some ACTs, is on the rise and a new alternative is urgently needed. Pyramax can help fill that urgent need and the positive opinion will help ensure its availability in areas where other ACTS are failing. Our next step is to ensure that healthcare workers understand how to appropriately use the drug. We will also work to complete development of paediatric formulations of this new combination.”

Initially, Pyramax will be registered in countries with areas of low malaria transmission where there is reported artemisinin resistance and diminished efficacy of other ACTs. It will be an important additional tool for WHO’s artemisinin resistance containment strategy in these countries, where its use will also facilitate the collection of more information on this combination. As liver enzyme elevations were noted in some subjects, until further data after retreatment is obtained, it is recommended that Pyramax be administered not more than once.

Taking over the project from WHO/TDR in 2002, when Pyramax was entering preclinical trials, MMV embarked on a partnership with Shin Poong. Since then, the partnership has taken the drug through early clinical studies leading to four successful, pivotal Phase III clinical trials with over 3,500 patients in 18 countries in sub-Saharan Africa, Southeast Asia and India. In addition, safety and efficacy has been confirmed for the Pyramax paediatric granules formulation in children as young as 6 months and work is on-going to submit the dossier in the near future.

“The managerial decision to commence the Pyramax project was based on Shin Poong’s core values and company policies, which have guided us for nearly half a century,” said Mr. Chang Kyun Kim, President of Shin Poong. “It represents an effort to fulfil our corporate social responsibilities and to realize universal values. To advance these values, Shin Poong will extensively collaborate with the
WHO to register *Pyramax* in malaria-endemic countries and supply *Pyramax* at an affordable price so that many lives, especially those of children, can be saved and the general public’s health can be maintained.”

Disclaimer

This document contains certain forward-looking statements that may be identified by words such as ‘believes’, ‘expects’, ‘anticipates’, ‘projects’, ‘intends’, ‘should’, ‘seeks’, ‘estimates’, ‘future’ or similar expressions, or by discussion of, among other things, vision, strategy, goals, plans, or intentions. It contains hypothetical future product target profiles, development timelines and approval/launch dates, positioning statements, claims and actions for which the relevant data may still have to be established. Stated or implied strategies and action items may be implemented only upon receipt of approvals including, but not limited to, local institutional review board approvals, local regulatory approvals, and following local laws and regulations. Thus, actual results, performances or events may differ from those expressed or implied by such statements.

We ask you not rely unduly on these statements. Such forward-looking statements reflect the current views of Medicines for Malaria Venture (MMV) and its partner(s) regarding future events, and involve known and unknown risks and uncertainties.

MMV accepts no liability for the information presented here, nor for the consequences of any actions taken on the basis of this information. Furthermore, MMV accepts no liability for the decisions made by its pharmaceutical partner(s), the impact of any of their decisions, their earnings and their financial status.

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Notes for Editors

Article 58 of Regulation (EC) No 726/2004 was created in 2004. Technically, it establishes a mechanism for the EMA to give a scientific opinion, in cooperation with the World Health Organization (WHO), for the evaluation of medicinal products intended exclusively for markets outside the (European) Community (Regulatory Reference, s.d.).

Reference
Safety and Efficacy Statement

The safety and efficacy of Pyramax® was established in clinical studies involving more than 3,500 patients aged 4 months to 60 years. Four pivotal Phase III studies with Pyramax (180:60 mg for the tablet formulation and 60:20 mg for the granule formulation) have been completed in disease-endemic countries in sub-Saharan Africa and Asia:

- Two studies compared the efficacy and safety of Pyramax with those of artemether-lumefantrine (AL) in subjects with acute uncomplicated *P. falciparum* malaria; one of these was conducted in subjects ≤12 years of age the other in subjects 3 to 60 years of age, inclusive.
- A third study compared the efficacy and safety of Pyramax with that of the loose combination of mefloquine (MQ) + artesunate (AS) in subjects 3 to 60 years of age, inclusive, with acute uncomplicated *P. falciparum* malaria.
- A fourth study compared the efficacy and safety of Pyramax with that of chloroquine in subjects 3 to 60 years of age, inclusive, with acute uncomplicated *P. vivax* malaria.
- A fifth, smaller study in Republic of Korea compared the efficacy and safety of Pyramax with that of chloroquine in subjects 3 to 60 years of age, inclusive, with acute uncomplicated *P. vivax* malaria.

In the *P. falciparum* studies the primary end point was PCR-corrected ACPR (adequate clinical and parasitological response) on Day 28 in the per-protocol (PP) population. The PCR-corrected ACPR at Day 28 was 99.2% with Pyramax compared to 98.1% with MQ + AS loose combination in one trial, 99.5% for Pyramax compared to 99.2% for AL in a second trial, and 97.6% for Pyramax compared to 98.8% with AL in a third trial. In each of these 3 studies, non-inferiority of Pyramax vs. the comparator was demonstrated for the PCR-corrected ACPR on Day 28 in the EE (efficacy evaluable) population. The non-inferiority of Pyramax to comparators was demonstrated through Day 42.

In the *P. vivax* study, crude cure rate on Day 14 in the PP population was the primary end point. Non-inferiority of Pyramax (cure rate 99.5%) compared with chloroquine (cure rate 100%) was demonstrated with respect to the crude cure rate on Day 14. The non-inferiority of Pyramax to chloroquine was demonstrated through Day 42. Pyramax was rapidly effective, with more than 90% of subjects clearing parasites and fever within 48 hours.

Treatment-emergent AEs reported for ≥5.0% of subjects in any treatment group across all Phase II/III studies were headache (10.6%) and cough (5.9%) in the Pyramax group; headache (10.4%) and dizziness (6.6%) in the MQ + AS group; cough (9.1%), headache (7.6%), abdominal pain (5.1%), and upper respiratory tract infection (5.1%) in the AL group; headache (14.4%) and myalgia (8.6%) in the chloroquine group.

Liver enzyme elevations were noted in some patients, but also after retreatment in a few healthy volunteers. As a result, until further data after retreatment is obtained, it is recommended that Pyramax be administered not more than once.
About MMV

MMV is recognized as the leading product development partnership (PDP) in the field of antimalarial 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 antimalarial drugs.

**MMV’s 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’s strength comes from its product development partnership (PDP) model reflected in its network of more than 170 pharmaceutical, academic and endemic-country partners in 45 countries. MMV also works in close partnership with a number of WHO programmes that include TDR, the Global Malaria Programme (GMP) and Roll Back Malaria (RBM).

MMV is currently managing the largest portfolio of antimalarial R&D projects ever assembled. In October 2011, Eurartesim® (dihydroartemisinin-piperaquine), an ACT developed in partnership with Sigma-Tau, was granted regulatory approval by the EMA and in November 2010, Guilin’s artesunate injection for the treatment of severe malaria was approved by the WHO’s Prequalification programme with assistance from MMV. In addition, Coartem® Dispersible (artemether-lumefantrine), a child-friendly version of the ACT Coartem®, was developed by Novartis in partnership with MMV and launched in 2009.

The key to MMV’s success lies in the focus of its mission, and the diversity of its team of almost 50 personnel from more than 20 countries, handpicked for their expertise and commitment to global health.

Since foundation, MMV has received financial support from the following donors: Bill and Melinda Gates Foundation; UK DFID; Rockefeller Foundation; Netherlands Minister Devt. Co-operation; WHO/RBM; Swiss Government (DEZA/SDC); World Bank; Wellcome Trust; ExxonMobil Foundation; BHP Billiton; USAID; EU CRIMALDDI; Irish Aid; National Institutes of Health (NIH); Spanish Agency for International Development; Newcrest Mining Limited.

[www.mmv.org](http://www.mmv.org)
About Shin Poong

Shin Poong Pharmaceutical Co. Ltd. was established in 1962, and has continued to make great strides in its contribution to improve the general public’s health by developing and distributing high-quality pharmaceutical products both locally and globally. Equipped with the utmost advanced facilities to meet "KGMP" (Korean Good Manufacturing Practice) and "BGMP" (Bulk Good Manufacturing Practice), Shin Poong is committed to the production of high-quality medical supplies and has developed the latest high-value medicines by continuously upgrading and improving the Shin Poong Central Research Institute (CRI).

The CRI was established in 1988 to embody the company motto, "For the health of the people". It consists of five research departments: Synthesis, Materials, Bio-engineering, Pharmacology and Analysis with 50 researchers dedicated to developing efficacious pharmaceutical products for the future. The CRI focuses on the development of pharmaceutical products, and has significantly contributed to the technical development and growth of the Korean pharmaceutical industry. To remain at the cutting-edge of technical development, Shin Poong constantly share ideas with various entities around the world.

Since its establishment 50 years ago, Shin Poong has built up a culture focused on drug development motivated by corporate social responsibility. As an illustration, in 1976 Shin Poong developed the first generic version of Mebendazole for the treatment of worm infections. Following this success, Shin Poong focused on the development of medicines for schistosomiasis (also known as Bilharzia). At the time, it was estimated that several hundred million people were suffering from schistosomiasis across Africa, Asia and parts of Latin America. Furthermore, the company successfully developed an optimized process of raw material production and effective formulation of Praziquantel. The aforementioned successes enabled Shin Poong to deliver the appropriate medicines at an affordable price to the people in need. Since then, Shin Poong has been a reliable supplier of these medicines for various institutions and entities such as WHO, Unicef, IDA, and other not-for-profit organizations in the field of neglected diseases.

Shin Poong’s core values and prior experience lead the company to commence the Pyramax development project in 1999. Shin Poong established production facilities in Ansan, Korea exclusively for both the active pharmaceutical product and finished dosage forms of Pyramax with state-of-the-art technology. The facilities have obtained Good Manufacturing Practice certifications from EMA as well as Korean FDA. The facilities have also been designed to be able to expand to meet future increases in demand.

www.shinpoong.co.kr/engshin/mainFrameset.htm