PRESS RELEASE

Embargoed until 13.00h CET, Wednesday, 20 April 2016

Pyramax® granules (pyronaridine-artesunate) for children added to WHO list of prequalified medicines

Geneva, 20 April 2016. Pyramax® granules (pyronaridine-artesunate) for the treatment of uncomplicated malaria in children from 5-20kg was added to the World Health Organization's (WHO) list of prequalified medicines in March 2016. This follows the European Medicines Agency's (EMA) decision to grant the medicine a positive scientific opinion through its Article 58 procedure in November 2015 – making *Pyramax* granules the first fixed-dose artemisinin combination therapy (ACT) developed specifically for children to be granted this opinion through article 58.

Simultaneous with its review of *Pyramax* granules, the EMA also authorized significantly expanded use of *Pyramax* tablets for patients >20kg. While this medicine was first granted a positive scientific opinion by the EMA in 2012, the new label expands the possibility of *Pyramax's* deployment in all malaria-endemic countries, allowing for repeated treatments.

Pyramax is the result of a product development partnership between Medicines for Malaria Venture (MMV), and Shin Poong Pharmaceutical Co. Ltd., Republic of Korea. Beginning in 2002, this drug development programme led to the testing of *Pyramax* in over 3,500 malaria patients in clinical studies in 18 countries in Africa and Asia, in which the medicine has shown high efficacy – similar to existing WHO-recommended ACTs.

Following the EMA's initial positive scientific opinion in 2012, *Pyramax* was included in an extensive Phase IIIb /IV trial conducted by the West African Network for Antimalarial Drugs (WANECAM) from 2011–2016. Publication of a sub-analysis of the findings in the *Lancet Infectious Diseases* in October 2015[1] reconfirmed the safety and efficacy of *Pyramax*, even when re-dosed up to 8 times in a single patient over a 2-year follow-up period.

Pyramax's key attributes:

- In line with WHO's guidance on making Better Medicines for Children[2], *Pyramax* granules, was developed expressly for palatability and ease-of-use in children, the most vulnerable population facing the gravest risks from malaria.

[1] Sagara I *et al.* "Safety and effi cacy of re-treatments with pyronaridine-artesunate in African patients with malaria: a substudy of the WANECAM randomised trial." *Lancet Infect Dis* 16: 189–98 (2016).
[2] World Health Organization. "Better Medicines for Children", Report by the WHO 60th World Health Assembly Secretariat, April 2007 http://apps.who.int/gb/archive/pdf_files/WHA60/A60_25-en.pdf

- *Pyramax* is the only ACT included in the WHO list of prequalified medicines to have been evaluated in pivotal Phase III studies for efficacy in clearing *P. vivax* infections, in addition to *P. falciparum* infections.
- *Pyramax* has a long duration of action, which provides a useful period of post-treatment protection against reinfection.[3]
- *Pyramax* is a once-a-day medicine administered over 3 days.
- *Pyramax* is not subject to "food effects", meaning that its effectiveness is not impacted by the presence or absence of fat-containing drinks or solid foods.[4]
- *Pyramax* shows comparable efficacy to the four fixed-dose ACTs currently recommended by WHO[5] for curing uncomplicated malaria.

Pyramax tablets are currently approved in 14 countries in Asia and Africa. MMV and Shin Poong will work with partners to support further endemic-country registrations and first-time registration of *Pyramax* granules. In 2016, a Phase IV pharmacovigilance study will be initiated, generating additional data about *Pyramax's* use in real-life settings.

Quotes

"Malaria control is at a critical juncture," said David Reddy, MMV's CEO. "Since 2000 the number of clinical cases of malaria has fallen by 18% and the malaria mortality rate is estimated to have fallen by 60%. But we need new tools to continue winning in the fight against malaria. As the newest medicine designed specifically for the treatment needs of the youngest most vulnerable patients, *Pyramax* granules will make a critical contribution to curing patients and saving lives."

"We at Shin Poong are proud that our partnership with MMV has resulted in EMA and WHO inclusion of *Pyramax*, in the family of quality-assured antimalarial medicines" said Mr Won June Chang, CEO of Shin Poong. "We ventured into the *Pyramax* project guided by Shin Poong's core values to work for the health of people everywhere. We will now work with MMV to register both the tablets and granules of *Pyramax* in malaria-endemic countries and ensure uptake of this alternative and effective option."

"Pyramax presents an excellent addition to current ACTs," said Prof. Abdoulaye Djimdé, WANECAM Project Coordinator at MRTC, Bamako, Mali. "Not only can it be administered to patients of all ages from infants to adults, but it is easy to take, the patient requires no further treatment in 28 days, needs no additional monitoring and it can be given again to patients who suffer from repeated bouts of malaria. *Pyramax* will be a most welcome additional weapon for our fight against malaria"

---

[3] Tshefu AK *et al.* "Efficacy and safety of a fixed-dose oral combination of pyronaridine-artesunate compared with artemether-lumefantrine in children and adults with uncomplicated *Plasmodium falciparum* malaria: a randomised non-inferiority trial". *Lancet* 375: 1457–67 (2010).

[4] EMA Summary of Product Characteristics, Annex I.
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/06/WC500129288.pdf

[5] Artemether-lumefantrine. Artesunate-amodiaquine. Dihydroartemisinin-piperaquine. Artesunate-mefloquine. *WHO Guidelines for the Treatment of Malaria, 3rd ed, 2015, p. 9*

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.

For further information please contact:

Elizabeth Poll
Editor and Publications Officer
T: +41 22 555 03 17 | M: +41 79 907 59 92
Email: polle@mmv.org

Notes for Editors

Article 58 of Regulation (EC) No 726/2004 was created in 2004. Technically, it establishes a mechanism for the EMA to undertake a scientific assessment and provide guidance, in cooperation with the World Health Organization (WHO), for the evaluation of medicinal products intended exclusively for markets outside the European Union.

Regulatory Reference, n.d. *EMA Article 58.* [Online]
Available at:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000157.jsp
[Accessed 2 April 2016].

About MMV

MMV is a leading product development partnership (PDP) in the field of antimalarial drug research and development. Its mission is to reduce the burden of malaria in disease-endemic countries by discovering, developing and delivering new, effective and affordable antimalarial drugs.

Since its foundation in 1999, MMV and partners have developed and brought forward six new medicines: Coartem® *Dispersible* (artemether-lumefantrine), a child-friendly formulation developed with Novartis; Guilin's artesunate injection Artesun® for the treatment of severe malaria; Eurartesim® (dihydroartemisinin-piperaquine) with Sigma-Tau; Pyramax® and Pyramax® granules for children (pyronaridine-artesunate) co-developed with Shin Poong; and Guilin's sulphadoxine-pyrimethamine + artesunate amodiaquine (SP+AQ) for seasonal malaria chemoprevention, which received WHO prequalification with MMV's support. In addition, MMV has taken over the stewardship of two approved artemisinin combination therapies (ACTs) developed by Drugs for Neglected Diseases *initiative* (DND*i*) and partners – artesunate-amodiaquine (ASAQ) and artesunate-mefloquine (ASMQ).

Since 2009, over 300 million courses of *Coartem Dispersible* treatment have been supplied to 50 malaria-endemic countries; and since prequalification in 2010, an estimated 36 million vials of artesunate injection have been delivered, saving 200,000–240,000 additional lives.

MMV and partners manage a portfolio of 65 projects, the largest portfolio of antimalarial R&D and access projects ever assembled. The portfolio includes nine new drugs in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria, and drugs that could support the elimination/eradication agenda. MMV's success in research and access & product management comes from its extensive partnership network of over 400 pharmaceutical, academic and endemic-country partners in more than 55 countries.

MMV's vision is a world in which innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and ultimately help to eradicate this terrible disease.

http://www.mmv.org

About Shin Poong

The Shin Poong Pharmaceutical Co. Ltd. was established in 1962, and has continued to make great strides in their contribution to the improvement of people's health, not only by developing high-quality medicines but also distributing them locally and globally. With the facilities to meet "BGMP" (Bulk Good Manufacturing Practice), "KGMP" (Korean Good Manufacturing Practice) and "EU GMP" (European Union Good Manufacturing Practice), Shin Poong commits to producing high-quality medical supplies and has developed high-value new medicines by upgrading 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 six research departments: R&D planning and management, formulation, organic chemistry, biotechnology, and analysis and pharmacology. About 80 researchers are exerting their effort to develop a variety of pharmaceutical products from drug substances and drug products. The CRI focuses on development of innovative new drugs, incrementally modified drugs (IMD), biological products and generic products. While continuing to improve its own R&D capabilities, the company has sustained a close partnership among industry, academy and research to share ideas and efficiently introduce key technologies.

Shin Poong Pharmaceuticals has invested in the construction of a state-of-the-art manufacturing facility outside Seoul, to produce GMP *Pyramax* tablets and paediatric granules as well as other medicines.

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