PYRAMAX®

(PYRONARIDINE-ARTESUNATE)

A HIGH-QUALITY TREATMENT OPTION FOR *P. FALCIPARUM* AND *P. VIVAX* MALARIA

Pyramax:

- Provides a simple once-daily, 3-day treatment course
- Is the *only* ACT with a positive opinion from a stringent regulatory authority for the treatment of both *P. falciparum* and *P. vivax* malaria
- Is available in tablet form for adults and children over 20 kg and child-friendly granules for children from 5-20 kg
- Can be taken with or without food
- Has been successfully used for treating successive episodes of malaria, with repeat dosing intervals as short as 28 days
- Has a positive scientific opinion via EMA's Article 58 process and is thus cross-referenced in WHO's list of prequalified medicines, allowing it to be purchased with donor funds

Pyramax: increasing treatment options in malaria-endemic countries

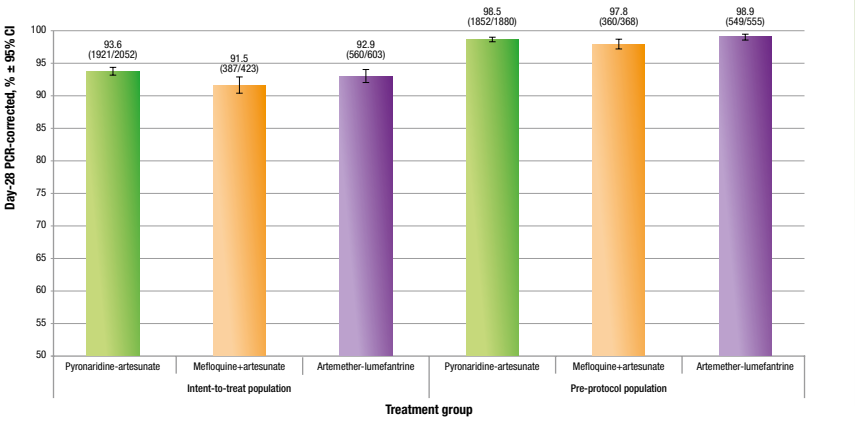
Since 2002, Shin Poong Pharmaceutical and Medicines for Malaria Venture (MMV) have worked in partnership to develop Pyramax®, a high-quality, novel fixed-dose artemisinin-based combination therapy (ACT) with a 2-year shelf life. In a rigorous clinical trial programme, *Pyramax* has been shown to be highly efficacious and active against both *P. falciparum* and *P. vivax* [1-3] – the two most prevalent malaria parasites.

In 2012, *Pyramax* became the first ACT to receive a positive scientific opinion for efficacy, tolerability and quality from the European Medicines Agency (EMA) under Article 58 for the treatment of a single malaria episode in areas of low endemicity and low transmission, with evidence of artemisinin resistance, for use by adults and children over 20 kg.[4]

New indication and a child-friendly presentation

Following EMA approval, *Pyramax* was the subject of an extensive phase IIIb/IV study testing the safety and efficacy of its repeat use in patients. In parallel, a new child-friendly granule presentation was developed. The data generated from this programme were instrumental in achieving a first-time positive opinion from the EMA in November 2015 for Pyramax® Granules for infants and children between 5 and 20 kg, as well as approval of a strengthened product label for the tablet. The new label allows for the repeat use of *Pyramax,* removing the previous restrictions that had limited its use.[4] The new indication,[5] together with the child-friendly formulation, means that *Pyramax* presents one of the most comprehensive options for treating acute uncomplicated malaria.

Day-28 PCR-corrected adequate clinical and parasitological response of three ACTs from 'Safety and efficacy of pyronaridine-artesunate in uncomplicated acute malaria: an integrated analysis of individual patient data from six randomized clinical trials'[6]



References

1. Poravuth Y *et al.* Pyronaridine-artesunate versus chloroquine in patients with acute *Plasmodium vivax* malaria: a randomized, double-blind, non-inferiority trial. *PLoS One* 6:e14501 (2011).
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5. Pyramax®/Pyramax® Granules Summary of Product Characteristics: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/06/WC500129288.pdf.
6. Sagara I *et al.* Safety and efficacy 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).

SHIN POONG PHARM. CO., LTD.
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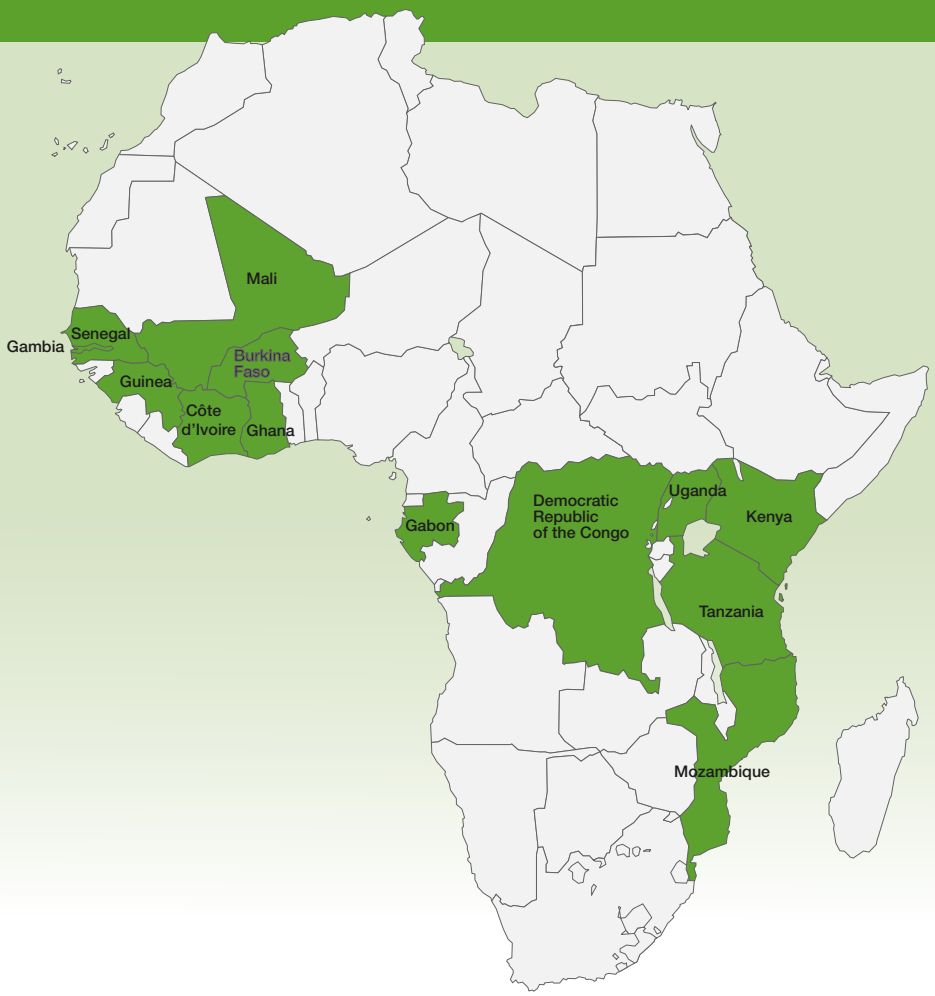
African countries where Pyramax® has been studied



"As the global health community intensifies elimination efforts there is a continued need for well-studied, high-quality antimalarial medicines. *Pyramax* is such a medicine. We are proud to have worked on the development of this important medicine with Shin Poong, Professor Abdoulaye Djimde and his fellow investigators in the WANECAM network. The results of this extensive research re-confirmed *Pyramax*'s efficacy and helped secure the EMA's positive scientific opinion of both the tablet and the granule formulation for children. With this approval in hand, MMV and Shin Poong will work together with endemic countries to pursue national approvals for *Pyramax*, making it available to the patients that need it."

Dr David Reddy, CEO, MMV

Efficacy and safety demonstrated in clinical trials

- In two phase III trials investigating *Pyramax* compared to artemether-lumefantrine (AL) or compared to mefloquine plus artesunate (MQ+AS)[7] in patients with uncomplicated *P. falciparum* malaria in Africa and Asia, the PCR-corrected adequate clinical and parasitological response rates at day 28 for *Pyramax* were 99.5% and 99.2%, respectively.
- In a phase 3 trial of *Pyramax* compared to chloroquine for the treatment of *P. vivax* malaria in Asia, the day-28 cure rate for *Pyramax* was 97.1%.[8]
- In a phase III trial of *Pyramax* Granules compared to AL crushed tablets in children with *P. falciparum* malaria the PCR-corrected adequate clinical and parasitological response rate at day 28 for *Pyramax* Granules was 97.1%.[9]
- Treatment-emergent adverse events (AEs) reported in ≥ 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.[10]
- In a phase IIIb/IV study led the West African Network for Clinical Trials of Antimalarial Drugs (WANECAM), *Pyramax* was re-dosed in patients for two or more treatments. The study concluded that the drug's efficacy and safety were similar on first malaria treatment and re-treatment of subsequent episodes, thus supporting wider use of *Pyramax* as an alternative treatment for malaria in sub-Saharan Africa.[6]

References

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