

The use of artesunate-pyronaridine for the treatment of uncomplicated malaria

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INFORMATION NOTE

This note aims to clarify any perceived contradiction between the inclusion of artesunate-pyronaridine in the WHO list of prequalified medicines for malaria and Model List of Essential Medicines, and the recommendations in the current WHO *Guidelines for the treatment of malaria* (2015).

Considering the positive scientific opinion of artesunate-pyronaridine under the European Medicines Agency (EMA)'s Article 58, its inclusion in the WHO list of prequalified medicines for malaria, Model List of Essential Medicines and Model List of Essential Medicines for Children, as well as the recently concluded review by the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP):

artesunate-pyronaridine can be considered a safe and efficacious artemisinin-based combination therapy (ACT) for the treatment of uncomplicated malaria in adults and children weighing 5 kg and over in all malaria-endemic areas. Countries can consider including this medicine in their national treatment guidelines, procure it, and monitor its safety and efficacy. Deployment should be conducted under a pharmacovigilance system as required for the introduction of all new medicines.

BACKGROUND

Artesunate-pyronaridine (Pyramax®), a fixed-dose ACT, is the first ACT to be specifically indicated for the treatment of both blood-stage *Plasmodium falciparum* and *P. vivax* following multicentre clinical studies in Africa and Asia.

In 2012, artesunate-pyronaridine was granted a positive scientific opinion under the EMA's Article 58 procedure, but with a restricted label, mainly due to concerns over potential hepatotoxicity of the pyronaridine component, efficacy in children under 5 years of age, and safety, especially with repeat dosing.

In 2015, an EMA Scientific Advisory Group concluded that cumulative safety data on hepatic events had provided sufficient evidence to alleviate concerns over hepatotoxicity and thus to allow recommendation of the use of artesunate-pyronaridine for the treatment and re-treatment of uncomplicated malaria in patients without signs of hepatic injury (including children weighing 5 kg and over). The EMA therefore modified the product label to remove all restrictions on repeat dosing, on use only in areas of high antimalarial drug resistance and low malaria transmission, and on requirements to monitor liver function. In addition, it granted a positive scientific opinion for artesunate-pyronaridine granules for the treatment of children with a body weight of 5–20 kg.¹

Artesunate-pyronaridine was included in WHO's list of prequalified medicines for malaria in April 2012, based on the EMA's positive scientific opinion of this product in accordance with Article 58. Since labelling provisions are based on EMA conclusions, these provisions were updated as a result of the EMA's 2015 review.

Products included in the WHO prequalification list are those that have been assessed through the various mechanisms and found to comply with WHO-recommended regulatory standards and requirements for quality, safety and efficacy.

In June 2017, artesunate-pyronaridine was also added to the WHO Model List of Essential Medicines and Model List of Essential Medicines for Children.

Due to the hepatotoxicity concerns identified in 2012, the WHO *Guidelines for the treatment of malaria* (2015) did not recommend the use of artesunate-pyronaridine for general use. A further meeting in December 2017 resulted in the need for the Global Malaria Programme to request, in 2018, the support of the WHO ACSoMP to conduct an independent expert review of all available data and information. Having completed its review recently, the committee considered that the current safety restrictions on the use of artesunate-pyronaridine (Pyramax®) for the treatment of uncomplicated malaria, as stated in the *Guidelines for the treatment of malaria*, are no longer justified.²

In due time, the Global Malaria Programme will revise the *Guidelines for the treatment of malaria* based on new information available.

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Endnotes

- 1 https://www.ema.europa.eu/en/documents/medicine-outside-eu/pyramax-product-information_en.pdf
- 2 https://www.who.int/medicines/regulation/medicines-safety/publications/ACSoMP_16.pdf