

ASMQ
FDC

Artesunate + Mefloquine

Fixed-Dose Combination

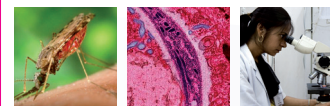
An easy to use,
highly efficacious
and affordable therapy
to fight malaria



Cipla

DNDi

Drugs for Neglected Diseases initiative



Malaria threatens approximately 3.3 billion people – half of the world's population – in 106 endemic countries. The World Health Organisation (WHO) estimates that in 2010, there were 216 million cases worldwide, 91% of which were due to *Plasmodium falciparum*, and that malaria caused the death of approximately 655,000 people, 86% of which were children under the age of five.⁽¹⁾

The WHO recommends five **Artemisinin-based combination therapies (ACTs)** for the treatment of uncomplicated *P. falciparum* malaria.⁽²⁾ Fixed-dose combinations (FDC) are strongly preferred and recommended over blistered co-packaged or loose tablets combinations, to promote adherence to treatment and to reduce the potential selective use of the medicines as monotherapy, which can cause resistance to develop.



One of the best documented treatments for malaria, the combination of artesunate (AS) and mefloquine (MQ), has been widely used in Asia over the past 20 years, and has been shown effective and safe in the treatment of uncomplicated *P. falciparum* malaria. To address the treatment needs of people affected by malaria, the FACT (Fixed-dose ACT) Consortium, created by DNDi and the WHO Special Programme for Research and Training in Tropical Diseases (WHO/TDR), developed the **artesunate-mefloquine fixed-dose combination (ASMQ FDC)** in a partnership with Farmanguinhos, a Brazilian government-owned pharmaceutical company, and, following a South-South technology transfer, with Cipla Ltd, an Indian pharmaceutical company. ASMQ FDC, produced by Cipla Ltd, was prequalified by WHO in September 2012, a recognition of the product's quality and an important step in accelerating access to the drug for patients. In addition, ASMQ FDC is currently registered in Brazil, India and Malaysia.

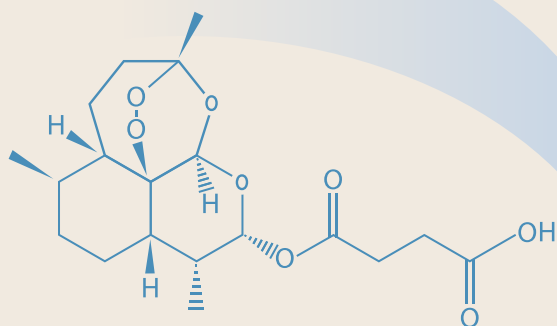
ASMQ FDC is safe, convenient and highly effective and its deployment in countries that have already adopted the combination of AS and MQ as first-line treatment will be of immediate benefit for patients. In addition, ASMQ FDC could also be useful in other countries in Asia, Latin America and Africa.

(1) WHO World Malaria Report, 2011

(2) WHO Malaria Treatment Guidelines, 2nd Edition, 2010

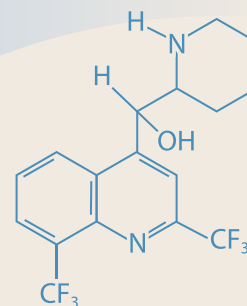
Fixed dose combination of 2 powerful molecules

Artesunate



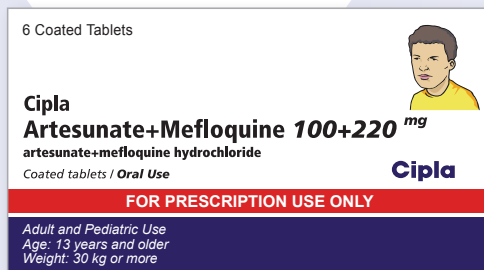
- Very high killing rates
- Rapidly absorbed
- Well tolerated

Mefloquine



- Drug of choice for multi drug resistant Malaria
- Consistently reported to show high treatment efficacy

**ASMQ
FDC**



ASMQ FDC
as easy to use
as **1** **2** **3**!

1 dose **2** products **3** days

One single daily dose of **1** or **2** tablets of **two** highly effective combined products for **three** days of affordable medicine

Keeping in line with Cipla's ethos of "Access to medicine for all", ASMQ FDC will be made available by Cipla Ltd at an affordable price of USD 1.5 to 3.0 (depending on dosing) for the public sector.

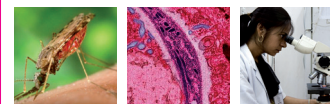
ASMQ FDC demonstrated high cure rate and good efficacy in a number of studies in Asia and Latin America, including a large intervention study in Brazil with over 23,000 patients.^[3] In a study comparing 5 ACTs in Myanmar, ASMQ FDC showed the highest cure rates, the lowest rates of gametocyte carriage (which are believed to affect the transmissibility of malaria) and provided the best post-treatment suppression of malaria.^[4] Greater coverage of effective drug treatments with more potent transmission-blocking activity is expected to result in greater effects on malaria incidence.

ASMQ FDC is well tolerated. The 2010 WHO malaria guidelines acknowledge that "side effects, where this [ASMQ] ACT has been deployed, were seldom debilitating and it has been well tolerated". No serious adverse events were reported during the study in Brazil that included over 23,000 patients, including children.

ASMQ FDC is designed to ensure treatment adherence and decrease the risk of emergence of resistance. In addition to increased compliance, its major benefits are an optimised short-term gastro-intestinal tolerance, the gametocytocidal effects of the artemisinin derivative and the prophylactic effect of mefloquine. These effects, combined with the long half-life of mefloquine, could have a significant impact on transmission.

[3] Santelli A, Ribeiro I, Daher A, et al. Effect of artesunate-mefloquine fixed-dose combination in malaria transmission in amazon basin communities. *Malaria Journal* 2012;11:286

[4] Smithuis F, et al. Effectiveness of five artemisinin combination regimens with or without primaquine in uncomplicated *falciparum* malaria: an open-label randomised trial. *The Lancet Infectious Diseases*, Volume 10, Issue 10, October 2010, Pages 673-681



Easy-to-use ASMQ FDC offers a quality, convenient, safe, and highly effective drug.

















Easy-to-use for children & adults:

- One single daily dose of 1 or 2 tablets of
- Two highly effective combined products for
- Three days of affordable medicine

Dosage adapted to age and weight

ASMQ FDC tablets of AS + MQ (25/55 mg and 100/220 mg) are offered in 4 dosage forms based on a weight-for-age reference. With age-based dosing, patients are more likely to receive the dose they need.

Recommended Dosage for ASMQ FDC Tablets – Asia

Weight (Kg)	Age	Recommended Dose	Day 1	Day 2	Day 3
 5 – 8	6 – 11 months	One Tablet 25/55 mg ¹ daily for 3 days			
 9 – 17	1 – 6 years	Two Tablets 25/55 mg ¹ daily for 3 days			
 18 – 29	7 – 12 years	One Tablet 100/220 mg ² daily for 3 days			
 > 30	> 13 years	Two Tablets 100/220 mg ² daily for 3 days			

¹ Mefloquine HCl 55 mg are equivalent to 50 mg of mefloquine

² Mefloquine HCl 220 mg are equivalent to 200 mg of mefloquine

The FACT Project Consortium: A Worldwide Collaboration to Develop and Deliver ASMQ

In 2002, in order to address the treatment needs of people most threatened by malaria, the FACT Consortium developed ASMQ as a FDC. Key partners include the Instituto de Tecnologia em Fármacos of Farmanguinhos/Fiocruz, Mahidol University, Université Victor Segalen Bordeaux 2 (TROPICAL), University of Oxford, Universiti Sains Malaysia, the Shoklo Malaria Research Unit, the Mae Sot Clinic, MSF, DNDi, and Cipla Ltd. Originally scaled up by Farmanguinhos, ASMQ FDC production was successfully transferred to Cipla Ltd in 2010.

Funding: The development of ASMQ FDC was supported by EU's INCODEV FP5, French AFD, Dutch DGIS, Spanish AECID, Swiss SDC, UK DFID, the European Commission's EDCTP, MSF, and the Wellcome Trust, UK.

Cipla Ltd

Cipla Ltd is a prominent Indian pharmaceutical company, actively engaged in manufacturing and exporting bulk drugs and finished products, and best known for manufacturing low-cost anti-AIDS drugs for HIV-positive patients in developing countries. Cipla has a wide portfolio with over 2,000 products ranging from cardiovascular to cancer, AIDS, malaria, asthma, diabetes, arthritis, diabetes and many other health conditions. Manufacturing facilities - 34 in India - have approvals from various regulatory agencies, including FDA (USA), WHO (Geneva), the MHRA (UK), MCC (South Africa), TGA (Australia) and PIC (Germany). Products are regularly sold to around 170 markets across the globe, in addition to catering for the domestic market.

www.cipla.com

DNDi

Founded in 2003, DNDi (Drugs for Neglected Diseases *initiative*) is a needs-driven, not-for-profit product development partnership (PDP) working to research and develop new treatments for neglected diseases such as sleeping sickness (human African trypanosomiasis), leishmaniasis, Chagas disease and malaria. DNDi drew founding partners primarily from the public sector in neglected disease-endemic countries: the Oswaldo Cruz Foundation in Brazil, the Indian Council for Medical Research (ICMR), the Kenya Medical Research Institute (KEMRI) and the Ministry of Health in Malaysia, along with Médecins Sans Frontières (MSF), the Institut Pasteur, and the WHO/TDR that acts as permanent observer. Since its inception, DNDi has developed 6 treatments, including two fixed-dose ACTs (artesunate + amodiaquine and ASMQ) for the treatment of malaria.

www.dndi.org