THE MALARIA PARTNERSHIP NEWSLETTER
NOVEMBER 2009

ASAQ is now registered **in 24 African countries.** In 2009, the first full year after prequalification by the WHO, **over 20 million malaria episodes** will have been **treated with ASAQ.**

ASAQ* FIELD MONITORING PROGRAM: AN AMBITIOUS PLAN TO ASSESS EFFICACY AND SAFETY IN REAL LIFE CONDITIONS

ASAQ is now registered in 24 African countries

ASAQ (Artesunate-Amodiaquine Winthrop®/Coarsucam®), the fixed-dose combination of artesunate and amodiaquine developed by sanofi-aventis and the Drugs for Neglected Diseases initiative (DNDi), was first registered in 2007 for the treatment of uncomplicated *P. falciparum* malaria. It received WHO prequalification in 2008.

ASAQ field monitoring program: Learning from real-life experience

Like all new medicines, ASAQ was registered based on data from controlled clinical trials. However, the full efficacy and safety profile for a new medicine may not be detected in clinical trial settings. In addition, pharmacovigilance and resistance monitoring systems in many sub-Saharan African countries need to be developed. For these reasons, sanofi-aventis and DNDi decided in 2007 to set-up proactive monitoring of ASAQ's efficacy and safety in real life conditions: **the ASAQ field monitoring program.**

This program is designed to generate high-quality scientific data in a variety of settings. It includes several studies throughout Africa that each provide specific sets of data on ASAQ safety and efficacy. This program aims to provide documentary answers to questions regarding ASAQ and other antimalarials, and three questions in particular. We know that many malaria patients suffer multiple episodes every year: how safe are repeated doses of antimalarials? Many treated patients do not have a confirmed diagnosis of malaria: how safe are antimalarials for these patients? Regarding efficacy, what is the impact of using a single artemisinin-based combination therapy in a given geographic area on the development of resistance?

The ASAQ field monitoring program includes a variety of studies that address one or several of these questions, through specific designs: randomized controlled trials, cohort studies, implementation programs, etc. Most of these studies are set up by sanofi-aventis or DNDi, others by academic or government institutions. All the available data will be entered in a single database to enable more detailed analyses in this larger dataset.

With over 20,000 malaria episodes being treated with the ASAQ fixed-dose combination, this is the most ambitious proactive drug monitoring program ever launched in Africa, for any drug. The WHO Department of Medicines Policy and Standards has expressed interest in seeing this program formalized as a Risk-Management Plan for ASAQ, the first to be submitted to the WHO. The experience gained should be useful to design Risk Management Plans for future antimalarials that will be launched with relatively limited sets of safety and efficacy data.

Working with partners

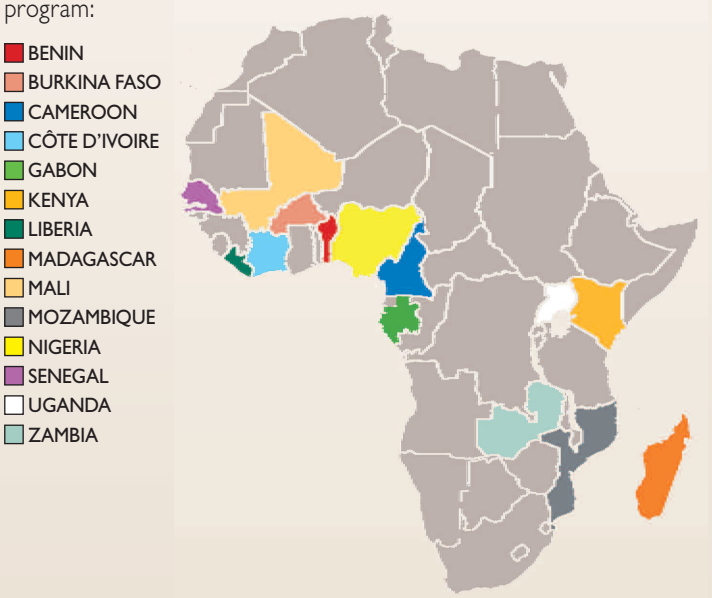
The ASAQ field monitoring program is set up in close collaboration with each country's National Malaria Control Program, and many scientific experts. DNDi has been sanofi-aventis' partner in this program from the outset. We are proud that Medicines for Malaria Venture (MMV) has recently joined this partnership and is supporting the largest study in this program, in Côte d'Ivoire, designed to involve more than 15,000 patients.

A first step, to build capacity

Beyond ASAQ, lessons learned from this program will facilitate the development of new pharmacovigilance and resistance monitoring methods in Africa that are suited to countries' needs and circumstances.

Covering a wide area

Countries with studies that contribute to the ASAQ field monitoring program:



** AS = artesunate, AQ = amodiaquine in a fixed-dose combination. See summary of product characteristics provided with this document.*

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ASAQ IDENTITY CARD

The partners, the vision

ASAQ is the only fixed-dose antimalarial combination of artesunate (AS) and amodiaquine (AQ) prequalified by the WHO. It was developed through an innovatory model of public-private partnership formed between sanofi-aventis and DNDi. The partners' objective was to develop a fixed-dose combination that would:

- ✔ Meet the WHO requirements
- ✔ Be adapted to the needs of African patients, especially those of children
- ✔ Be affordable
- ✔ Be non-patented

These objectives have been achieved, allowing ASAQ to become available in the field. ASAQ fits with WHO treatment guidelines, it has a simple dosing regimen (1 tablet a day up to 13 years of age, 2 tablets a day from14 years). Tablets can be dissolved in water, making it easier to treat patients, especially small children.

Making ASAQ affordable

ASAQ is available under the name Artesunate-Amodiaquine Winthrop® on the public market and under its brand name Coarsucam® on the private market. We apply a tiered-pricing policy, selling ASAQ at cost to public bodies, while Coarsucam® is sold on the private market at profit. This policy ensures the long-term sustainability of our economic model and enables us to develop added services and complementary tools that are also critical to combat malaria.

Local production, international expertise

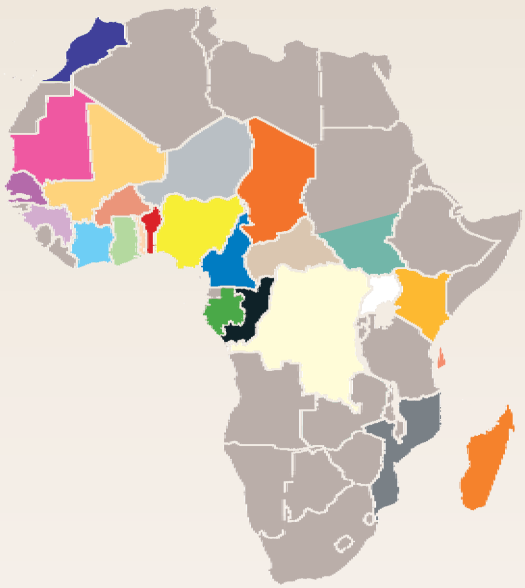
Sanofi-aventis' factory in Casablanca, Morocco, is certified for Good Manufacturing Practices by the WHO. It has the capacity to produce 70 million Artesunate-Amodiaquine treatments per year.

Number of treatments distributed

Each ASAQ treatment is sufficient to treat one malaria episode. In 2009, the first full year after prequalification by the WHO, we expect that over 20 million malaria episodes will have been treated with ASAQ.

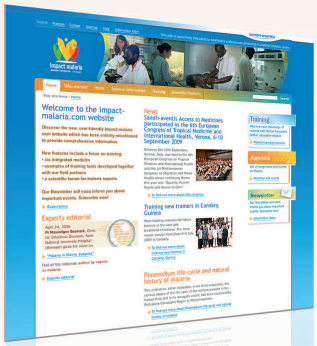
ASAQ is now registered in 24 countries in Africa, and now also in India

- BENIN
- BURKINA FASO
- CAMEROON
- CENTRAL AFRICAN REPUBLIC
- CHAD
- CONGO
- CÔTE D'IVOIRE
- DEMOCRATIC REPUBLIC OF CONGO
- GABON
- GHANA
- GUINEA
- KENYA
- MADAGASCAR
- MALI
- MAURITANIA
- MOROCCO
- MOZAMBIQUE
- NIGER
- NIGERIA
- SENEGAL
- SOUTH SUDAN
- TOGO
- UGANDA
- ZANZIBAR



More information

www.impact-malaria.com



www.dndi.org

Recent publications on ASAQ

- *Randomized, multicentre assessment of the efficacy and safety of ASAQ – a fixed-dose artesunate-amodiaquine combination therapy in the treatment of uncomplicated Plasmodium falciparum malaria.* JL Ndiaye, et al. Malaria Journal 2008, **8**:125
- *Tolerability and pharmacokinetics of non-fixed and fixed combinations of artesunate and amodiaquine in Malaysian healthy normal volunteers.* V. Navaratnam, et al. Eur J Clin Pharmacol 2009, **65**:809-821
- *The efficacy and safety of a new fixed-dose combination of amodiaquine and artesunate in young African children with acute uncomplicated Plasmodium falciparum.* S. Sirima, et al. Malaria Journal 2009, **8**: 48.
- *Population pharmacokinetics of artesunate and amodiaquine in African children.* K. Stepniewska, et al. Malaria Journal 2009, **8**:200.
- *Bioavailability of a co-formulated combination of amodiaquine and artesunate under fed and fasted conditions.* S. Fitoussi, et al. Arzneimittelforschung 2009, **59(7)**:370-376
- *Comparison of Sulfadoxine-Pyrimethamine, Unsupervised Artemether-Lumefantrine, and Unsupervised Artesunate-Amodiaquine Fixed-Dose Formulation for Uncomplicated Plasmodium falciparum Malaria in Benin: A Randomized Effectiveness Noninferiority Trial.* JF Faucher, et al. JID 2009, **200**:57-65

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