Malaria Initiative: Treatment

Starting with the patient

For over a decade, Novartis has been at the forefront of the change in the treatment of malaria from monotherapies to artemisinin-based combination therapies (ACTs). Novartis was the first to launch a fixed-dose ACT and was also the first to develop a dispersible ACT tailored to meet the needs of children*, one of the populations most vulnerable to malaria1.

* Infants and children weighing 5 kg to less than 35 kg and 12 years of age or less.
Turning an ancient remedy into a modern treatment

With the launch of Coartem® (artemether-lumefantrine, AL) in 1999, Novartis pioneered a high-quality antimalarial therapy that has become a standard of care for millions of patients around the world.

The development of Coartem® began in the 1990s when Novartis joined forces with Chinese partners to transform a traditional herbal remedy, used for centuries to control fevers, into a modern antimalarial medicine for the treatment of acute, uncomplicated Plasmodium falciparum malaria, responsible for most deaths from malaria.

Coartem® was the first fixed-dose ACT brought to market, and the first ACT prequalified by the World Health Organization (WHO) in 2004. The efficacy of Coartem® has achieved 28-day PCR-corrected cure rates of >95%, and the efficacy and safety of the product has clearly been demonstrated over the past 17 years in a clinical development program, life cycle management as well as real life use.

Coartem® combines artemether, a derivative of artemisinin (which is the extraction product of the sweet wormwood plant Artemisia annua) with lumefantrine in a single pill. As lumefantrine has never been deployed as a monotherapy, the potential risk of resistance to this compound may be lower than with other agents.

Approved in more than 60 countries, Coartem® is currently the only ACT also approved by the US Food and Drug Administration in 2009.

In 2015, the new dosage strength Coartem® 80/480**, which reduces the pill burden from 24 to 6 tablets, received WHO prequalification. This makes it the first artemether-lumefantrine (AL) with a reduced pill burden available for public sector procurement.

Responding to the unmet medical needs of children

More children die from malaria than any other patient group – every 2 minutes a child dies from malaria in Africa.

Ahead of the call from the WHO and UNICEF for “child-size” medicines, Novartis had started developing, in collaboration with Medicines for Malaria Venture (MMV), a sweet-tasting ACT specifically for children. Launched in 2009, Coartem® Dispersible is now approved in more than 40 countries and more than 300 million treatments have been delivered without profit in five years.

Coartem® Dispersible contains the same concentration of active ingredients as the regular tablet but in a dispersible formulation that is easier to give to babies and children, which helps to ensure this population receives the correct dose.

Clinical studies were performed to evaluate palatability, a key element in the acceptability of medicines by children. A sweet taste was selected to mask the bitter taste of lumefantrine, which is typical for antimalarials.

In an effort to enhance understanding of the treatment and promote adherence to therapy in areas where the population may not yet be fully literate, packaging featuring pictograph instructions was developed. The Novartis Malaria Initiative worked with PSI, a global health organization with programs targeting malaria, the Zambian Nurses Association, the University of

“In the earliest days, it was a small research project in partnership with Chinese scientists. Out of that project came one of the best drugs ever developed to combat malaria.”

Dr. Professor William Rodriguez, Research Associate, Harvard Medical School
Oslo, the KEMRI-University of Oxford-Wellcome Trust collaborative program, MMV and the WHO to develop this innovative packaging – which received the “Drug Packaging Design Award” from the Healthcare Compliance Packaging Council in 2009.

In addition, the Novartis Malaria Initiative produced an educational story booklet specifically for children and their families that contains key information on the disease and its treatment. The booklet has been translated into several languages.

**Advancing global public health**

In 2001, Novartis forged a groundbreaking public-private partnership with the WHO and later worked with several other partners such as UNICEF, the United States President’s Malaria Initiative, UNDP, MSF and international procurement agencies to provide Coartem® without profit for use by public health systems in developing countries. Despite the end of the WHO agreement in May 2011, these collaborations have achieved remarkable milestones in advancing global public health in the past decade. Today, deliveries of Coartem® and Coartem® Dispersible treatments have passed 750 million, contributing to a significant reduction of the death toll from malaria. More than half of those treatments have been used by children under the age of 5, the majority of them in Africa.

Today, eight WHO pre-qualified AL combinations are available and AL accounts for the largest volume of ACTs delivered (73%). Novartis has completed one of the largest and fastest scale-ups in the industry: from 4 million treatments in 2004 to more than 64 million treatments delivered in 2015 to more than 60 countries. In the same timeframe, thanks to economies of scale in sourcing and manufacturing, the price for public-sector buyers was cut by half over the years.

Joint research continues at the Novartis Institute for Tropical Diseases, the Genomics Institute of the Novartis Research Foundation and the Swiss Tropical and Public Health Institute to discover new treatments. This led in 2010 and 2011 to the discovery of two new antimalarial compounds, each with a unique mechanism of action. Both compounds are currently in Phase 2 clinical trials. If successfully developed, they would be the first new antimalarials in many years not belonging to the artemisinin class, and provide a completely new option to treat the disease.

**Rewarding medical innovation**

In 2010, Novartis was awarded the *Prix Galien USA Award* in the category of the “Best Pharmaceutical Agent” for Coartem®. Considered to be the industry’s highest accolade for pharmaceutical research and development, the Prix Galien recognizes the scientific excellence necessary to develop innovative medicines.

Earlier, Professor Yiqing Zhou and his research team at the Microbiology and Epidemiology Institute in Beijing, China, were awarded the 2009 *European Inventor of the Year Award* in the “non-European” category for developing Coartem®.

In 2015, Dr Youyou Tu, was awarded the *Nobel Prize* in medicine or physiology for her discovery of artemisinin in 1972. This discovery led to the development of ACTs which revolutionized the treatment of malaria.
Health impact on the ground

Rwanda

*Rwanda*, which adopted Coartem® as first-line therapy in 2006, reported a significant decline in malaria incidence. Between 2005 and 2012, malaria morbidity decreased by 87%, while malaria mortality declined by 74%.²² This decrease is attributed to several measures, including the distribution of long lasting insecticidal nets (LLINs), and targeting high-burden districts with indoor residual spraying (IRS) and effective ACTs. In spite of this, Rwanda has unfortunately experienced an upsurge in malaria cases in 2009, 2012 and 2013. Nonetheless, with the significant reduction in malaria cases over the past 10 years, the country aims to achieve malaria pre-elimination status nationwide by 2018.²²

Ethiopia

Positive outcomes have also been reported in *Ethiopia*, where Coartem® was launched as first-line therapy in 2004. More than 64 million LLINs were distributed between 2005 and 2014.²³ As a result of these interventions, the prevalence of malaria parasitemia in Ethiopia is now 1.3%,²³ and the incidence of malaria deaths in children aged under 5 years was 12.6% in 2010/2011, compared with 21.1% in 2003/2004.²⁴ The country has set up an elaborate health extension program involving around 38,000 volunteers who visit individual households, teach them about sanitation, do rapid diagnostic tests and treat positive cases²⁵.

Senegal

Large-scale deployment of the Novartis ACT and rapid diagnostic tests (RDTs) began in 2007 in *Senegal* and progressed rapidly, leading to a 3% prevalence of parasitologically-confirmed malaria cases in 2009 (from 36% clinical cases in 2001)²⁶. The proportion of deaths attributable to malaria in children under 5 was also drastically reduced from 30% to 7% in the same timeframe, and by 2009, malaria accounted for 4% of all deaths in the country²⁶. To further reinforce the interventions and successes in the fight against malaria, in 2008, Senegal introduced a new type of health worker, the village malaria worker, who provides RDT testing and ACT treatment to patients in the household. Senegal, like Rwanda, hopes to achieve pre-elimination status with less than 5% malaria prevalence by 2018²⁶.

The Novartis Malaria Initiative

For over a decade, the Novartis Malaria Initiative has been a pioneer in the fight against malaria. Focused on treatment, access, capacity building and R&D, the initiative is the largest access-to-medicine program within Novartis measured by the number of patients reached annually. Together with our partners, and with our continued patient-centric approach, we are committed to the common goal of malaria elimination.

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References


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