Published: September 2009

The Affordable Medicines Facility-malaria (AMFm): The Global Fund's approach to combating Malaria in the developing world

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Malaria remains a leading cause of morbidity and mortality in the developing world. The World Health Organization (WHO) estimates that a child dies from malaria every 30 seconds. In 2006 there were an estimated 247 million cases of malaria, causing nearly one million deaths, mostly among African children (1).

Until recently chloroquine (CQ) was the treatment of choice in most malaria endemic areas due to its remarkable safety and efficacy profile and affordability. However, the unrelenting increase in CQ-resistant malaria parasites since their first detection in 1978 has resulted in CQ's demise as the gold standard of uncomplicated falciparum malaria treatment. Sulfadoxine-Pyrimethamine (SP) has been the usual successor to CQ as first line treatment, given its low cost and convenient single dose. However, the evolution of malaria into a multi-drug resistant disease with concurrent increases in malaria-related morbidity and mortality has resulted in a global public health crisis.

The global response has been to encourage the use of combination antimalarial alternatives, preferably including an artemisinin derivative. The artemisinins are a modern group of medicines (e.g. artesunate, artemether, dihydroartemsinin, artemotil) derived from the ancient Chinese medicine Qinghaosu (isolated from the plant Artemisia Annua). These medicines have been shown to be remarkably effective against even severe forms of the disease, in some reports even better than quinine while demonstrating a reasonably robust safety profile (2).

In 2001 The World Health Organization recommended the combination of an artemisinin derivative and a longer-acting antimalarial (such as lumefantrine, SP, mefloquine or amodiaquine) as preferred first line treatment for uncomplicated malaria (3). There is overwhelming evidence that the addition of an artemisinin derivative to another effective malaria treatment significantly reduces treatment failure, delays the emergence of resistance, and reduces carriage of the gametocyte (the sexual reproductive stage of the malaria parasite within the individual which is related to the infectivity of the individual) and thus potentially malaria transmission (3). In sub-Saharan Africa, where at least 60% of the world's malaria cases and 80% of malaria deaths occur, most national ministries of health have changed their treatment policies from CQ or SP-based monotherapy to artemisinin-based combination therapy, commonly referred to as ACT.

However, a report by a Committee of the Institute of Medicines titled: "Saving Lives, Buying Time", published in 2004 suggested that simply replacing CQ with ACTs would be insufficient as even in the best of times CQ did not reach everyone and resulted in at least a million preventable deaths per year (4). What was needed was an expanded access to effective treatment in order to "gain ground" against malaria.

The practical challenges of implementing these new treatment policies on a large scale while ensuring that they are used correctly in resource-limited settings are considerable. Without external funding neither governments nor consumers, who bear most of the cost, would be able to afford these better, albeit more costly medicines. Adequate and consistent access to ACTs has also been severely hampered by the lower cost and better access to ineffective therapies such as CQ, SP and artemisinin montherapies. Patients tend to seek treatment for fever and malaria preferentially outside the formal public sector. This is usually due to the need to travel long distances for care, long waiting times and the poor availability of these medicines in government clinics and hospitals. This has driven patients to access care at the less controlled private sector (5). In many of the malaria-endemic countries, the regulation of medicines is inadequate, resulting in uncontrolled markets and the sale of substandard and/or counterfeit medicines. In these relatively poorly regulated settings, safe, effective and good quality ACTs in the private sector are costly, sporadically available and often require a prescription from a doctor or pharmacist.

The Affordable Medicines Facility-malaria (AMFm) has evolved as a global response to the challenge of reducing malaria mortality and delaying resistance to artemisinin and its derivatives (6). Through an innovative approach of buyer co-payment, the Global Fund will reduce the sale price of ACTs to the public, private and not-for-profit sector. The expectation is that there will be a significant drop in the cost of ACTs to patients, to

approximately $0.20 - $0.50 per treatment course resulting in increased access to treatment among those most at risk and the preferential use of ACTs over marketed artemisinin-based monotherapies and other antimalarials that are no longer recommended for use. Phase I of AMFm will provide funding for 11 countries (Benin, Cambodia, Ghana, Kenya, Madagascar, Niger, Nigeria, Rwanda, Senegal, Uganda, United Republic of Tanzania) for 24 months.

National governments and regulators in these initial countries are also exploring regulatory mechanisms to make ACTs available at licensed retail outlets without a doctor or pharmacist's prescription. Consequently funders and national regulators will have a greater responsibility to monitor the safety and rational use of these medicines within this expanded access framework. Current knowledge suggests that the ACTs that are now recommended are known to have a good safety profile with a very low risk of serious adverse drug reactions (7). However, the safety implications of this widespread availability of affordable ACTs in the private sector are unknown and would need to be assessed through innovative safety surveillance mechanisms. This initiative therefore has the potential to also strengthen and expand on existing drug safety surveillance systems, which in most of the initial AMFm countries are still in their infancy.

To optimise the effectiveness of this scheme, the AMFm project also includes interventions such as public education and awareness campaigns to encourage the population to seek early treatment and to increase demand for high-quality, affordable, subsidized ACTs; training of accredited retailers on the correct, safe storage and supply of ACTs to patients with suspected malaria and the introduction and/or strengthening of drug safety monitoring activities to identify and minimize any risks of harm associated with widespread use of ACTs.

In order to ensure that the anticipated public health benefits of this funding strategy are realized while minimizing the risk of unintended harm, all countries will be encouraged to monitor public and private drug distribution systems to assure that subsidized antimalarials reach their intended targets. Furthermore, monitoring and surveillance measures will be implemented to monitor the effectiveness of drug regimens, treatment failures, the emergence of resistant strains; and the risk of adverse antimalarial drug effects.

Ultimately, the hope is that this innovative economic mechanism will considerably reduce the burden of malaria on the developing world and could potentially serve as an economic model for the global management of other diseases of the poor.

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