Malaria subsidy pilot soars, but some see turbulence ahead

KAMPALA, UGANDA — In 2010, a Kenyan drug importation and distribution company named Harley's Limited stopped ordering low-cost, mediocre malaria medications, and began ramping up its orders of high-quality ones—by about fourfold. Vinod Guptan, head of marketing at the Nairobi-based company, says demand shifted when the price of the best drugs dropped, making them cheaper for vendors, who passed the savings on to local consumers. The about-face in preference illustrates the strong influence of the Affordable Medicines Facility for malaria (AMFm), a radical program designed to shift the market for malaria drugs that now faces scrutiny for wielding too much force.

Amy Maxmen

Private matters: A private pharmacy in Tororo, Uganda sells AMFm-subsidized drugs.

A team convened by the US Institute of Medicine (IOM) developed the idea for the effort in 2004, when malaria morbidity rates were rising in developing countries in part because many people with the disease opted for chloroquine, despite widespread resistance to the decades-old drug, or for rudimentary 'monotherapy' treatments that contained only a single active ingredient, artemisinin. The group reasoned that patients would switch to the leading artemisinin-based combination therapies (ACTs) if they cost less than the alternatives at drug shops because of subsidies offered to importers at the top of the supply chain.

"The fact is that these are poor countries with poor public health systems," explains Kenneth Arrow, an economist at Stanford University in California and an author on the IOM report. "When I discovered that 70% of chloroquine was distributed commercially, I immediately came to the conclusion that ACTs would have to be distributed through the private sector if we wanted nearly universal coverage."

After much discussion, the AMFm was born as a three-year pilot program in 2010 under the auspices of the Geneva-based Global Fund to Fight AIDS, Tuberculosis and Malaria. Support for the first phase totaling $316 million came from the Seattle-based Bill & Melinda Gates Foundation, the UK's Department for International Development and money raised mainly through airline ticket fees by a UNITAID partnership with nine countries.

In providing co-payments for drug distributors in the private as well as the public domain, the AMFm represents the first large-scale medical aid initiative to partner directly with the unregulated commercial sector in sub-Saharan Africa, says AMFm Director Olusoji Adeyi. Traditionally, international organizations help the government-run public sector obtain ACTs, which they then provide for free or nearly free. In many countries, however, villagers purchase drugs from shops when public clinics are closed or far away or have no medicines in stock.

Now in the final year of its pilot phase, AMFm has altered the malaria drug distribution landscape. But some global health coordinators voice concerns about how dramatically the initiative has altered the supply chain and funneled ACTs into just a handful of the countries that need them. The scrutiny comes amid an independent evaluation of AMFm contracted by the Global Fund and conducted by ICF International, a Fairfax, Virginia–based consultancy, and the London School of Hygiene and Tropical Medicine. Launched in February 2010, the assessment will inform a decision about AMFm's future in November or December of this year.

The price is right

Inadequate malaria medications no longer cost far less than ACTs in at least six of the eight countries selected for AMFm support: Ghana, Kenya, Madagascar, Nigeria, Tanzania (including Zanzibar) and Uganda. Before the initiative, vendors sold ACTs for between $6 and $11. Now, at roughly $1 per dose, the drugs are cheaper than monotherapy and about the same price as chloroquine. "No one even wants those others anymore because ACTs work rapidly and cost the same," says Guptan. "In 2009, we used to sell around 15,000 to 20,000 ACT [treatment packs] a month, and by the end of 2011 the orders were up to 200,000."

Last year, about 60% of the world's estimated supply of ACTs was allocated through AMFm channels, *Nature Medicine* has learned. By August, aid organizations had begun to complain of delays. The Swiss pharmaceutical company Novartis informed one of the largest malaria programs, the US President's Malaria Initiative (PMI), that it could not quickly fill a request for 18 million treatment packs. Some nations, such as Somalia, needed the doses urgently before the rainy season began. (Rain creates puddles from which swarms of mosquitoes, the vectors for malaria, hatch.)

"There was a clear rush last year between March and July of big orders from AMFm," explains Andrea Bosman, a malaria program coordinator at the World Health Organization (WHO) in Geneva. "Several funding agencies signaled that manufacturers were unable to meet their demands, and in some cases the manufacturers could not accept new orders. We were really worried."

At the heart of the ACT supply issues lies the reliance on artemisinin, a natural compound derived from sweet wormwood *Artemesia annua,* which farmers must plant ten months before drug manufacturers can use it. Predicting artemisinin demand has never been simple, and last year manufacturers were unprepared for an onslaught of requests from AMFm-subsidized buyers, explains Adeyi. Unlike orders from aid organizations and governments often bogged down in bureaucracy, Adeyi says the private sector ordered drugs efficiently. "What we have demonstrated, is that products move far more swiftly in the commercial sector than in the public sector," he says. "But there is some

ideological discomfort with that among global health practitioners because of their tradition of favoring public-sector channels."

Delivering promises

In response to the turmoil last summer, the WHO held a meeting in Geneva on 8 September 2011 with representatives from relevant organizations and drug companies—including the Global Fund, PMI and Novartis. Ultimately, the group averted disaster by shifting orders among manufacturers, allocating donor funds from one country to another and requesting that the AMFm slows its approvals for subsidies. "We learned that there wasn't a worldwide shortage," says Bosman, "but that the balance between supply and demand is very tight."

Still, delays persist, says Jean-Marie Kindermans, an administrator in Paris at the nonprofit Doctors without Borders, which stocks ACTs at its clinics in 30 malaria-endemic countries. Kindermans says that, in early 2011, Novartis shipped packages of the common ACT coartem within five weeks. Now the drugs take at least two months to arrive.

Beyond these delays, some people find it disconcerting that so much of the ACT supply goes to AMFm countries even though they represent about a quarter of the countries in which more than 1,000 people die of malaria each year. "Some AMFm countries, like Madagascar, aren't ones with high endemicity," Kindermans says. Of 43 African countries with malaria, at least 26 have more cases than that island state. And Ghana, with approximately 2.6 million malaria cases, was chosen by AMFm rather than Burkina Faso, the Democratic Republic of Congo or Malawi, which according to 2010 WHO figures struggle with twice that number.

Critics also worry that some of the ACTs handled by private sector vendors were sold to consumers regardless of whether the buyers had a diagnosis. "Buyers in Zanzibar—an island where malaria is almost eliminated—ordered 241,000 AMFm-subsidized doses," says Mohga Kamal-Yanni, a health advisor in the UK at the international nonprofit Oxfam. "Given that this medicine has a short shelf life, will all of these ACTs truly be sold to people with malaria? The figures don't tally, and, because of this demand, there are shortages elsewhere in the market."

Leaning on levers

Now the AMFm applies a series of so-called 'levers' to rationally approve orders, making it unlikely that Zanzibar will receive AMFm-subsidized doses again, according to Adeyi. "We are learning lessons as we go," he says. To explore how the program would function, he explains that countries were chosen not only on the basis of their malaria burden, but also the countries' experiences with ACTs purchased through Global Fund grants, and the involvement of the private sector in drug deployment.

Some effects of the pilot were unexpected. For example, public hospitals in Ghana—which historically procure ACTs through the government and aid programs—have bought AMFm-subsidized drugs from private vendors. Adeyi says that this unprecedented phenomenon illustrates how much more efficient the AMFm system is. However, Kamal-Yanni worries that if public hospitals rely on the commercial sector, and prices go up, they'll be forced to cut parts of their health budget to buy ACTs.

Another consequence is that several local drug manufacturers have halted their operations, says James Tibenderana, technical director of the African branch of the Malaria Consortium partnership based in Kampala, Uganda. Rather than buying local, drug wholesalers prefer to purchase subsidized drugs from AMFm's list of seven permitted companies, only one of which resides in Africa. "ACT manufacturers outside of the AMFm are moving on to making other drugs, leaving fewer companies on the market," explains Tibenderana. "So if AMFm comes to an end, the only players that will be capable of providing ACTs are the ones who had been included in the program."

Larger questions loom over whether the program will continue, expand or terminate next year. Growers of sweet wormwood in China needed to know how many seeds to plant last November, but the official answer from the Global Fund about the fate of the program won't be out until this December. "The fact that so many people are left in the dark like this, I guess to me, that is what's most shocking," Bosman says.

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Where do artemisinin-based combination therapies go?

98 million (treatments)	AMFm (private-sector orders delivered in 2011)
92 million	Global Fund (public sector, estimated procurement in 2011)
69 million	Non–Global Fund, non-PMI public sector (estimated 2011 procurements)
32 million	PMI (estimated procurement in 2011)
8 million	Full-price private sector (estimated demand in 2011)

- AMFm 2011 data are from 11 January 2011 to 30 December 2011. The AMFm private-sector figure includes both the private for-profit and private not-for-profit deliveries, but excludes AMFm-funded public-sector deliveries and those delivered in Cambodia, which have been included in the premium private-sector estimate.
- Global Fund numbers include AMFmfunded public sector deliveries.
- Non–Global Fund numbers include the World Bank, the UK Department for International Development and others.
- PMI numbers here have been adjusted for 2011.
- All public-sector numbers (PMI, Global Fund, others) have a 25% disbursement delay factor applied to them.

ACT market data from Prashant Yadav, William Davidson Institute at the University of Michigan

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Combination of factors: Prices and availability affect consumer choice of malaria drugs.