DONOR STATEMENT ON URGENT ACTION REQUIRED TO ADDRESS ANTIMALARIAL DRUG RESISTANCE

CONTEXT

Widespread use of artemisinin-based combination therapies (ACTs), which combine artemisinin with a partner drug, have contributed to tremendous reductions in malaria cases and deaths over the past two decades. However, the recent emergence and spread of ACT drug resistance in Africa is now threatening progress and putting millions of lives at risk, forcing malaria endemic countries to stop or scale back other lifesaving malaria interventions in order to buy more costly ACTs.

It is in this context that we urgently call on bilateral and multilateral donors, philanthropic foundations, and the private sector to join us in heeding the call from malaria endemic countries to make existing alternative ACTs available and affordable.

THE CHALLENGE

The current standard of care for malaria treatment recommended by the World Health Organization (WHO) are ACTs. They have become the most common treatment in Africa, and are a major contributor to modern malaria control gains. ACTs were recommended by WHO in part to counter the threat of antimalarial drug resistance by combining antimalarials with different properties. Nevertheless, with ACTs in widespread use in sub-Saharan Africa for nearly two decades, evidence of resistance to the artemisinin component of ACTs has emerged in several locations, including Rwanda, Eritrea, Ethiopia, Tanzania, and Uganda.

In addition to the challenge posed by artemisinin resistance itself, declines in artemisinin efficacy also put more pressure on drugs paired with artemisinin. This threat is magnified by the fact that a single ACT – artemether-lumefantrine (AL) – accounts for over 85 percent of the public sector malaria treatment market and is the most common ACT in the private sector. Unsurprisingly, signs of reduced efficacy of AL are also now emerging across multiple sites in Africa, magnifying the urgency to address antimalarial drug resistance. The global malaria community must act now to diversify the ACTs in use to mitigate the spread of antimalarial drug resistance.

Other disease efforts have demonstrated that the key to preventing and addressing resistance is diversification of the medicines in use. Systematic approaches to diversification of antimalarial drugs in use, including adoption of multiple first-line therapies and consideration of antimalarial drugs used for chemoprevention, is critical for stewardship of current and future treatment options.

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Currently, alternative ACTs with excellent safety and efficacy profiles are available to help mitigate evolving antimalarial resistance. The two best options are: dihydroartemisinin-piperaquine (DP) and artesunate-pyronaridine (ASPY). However, both products are currently 3-4 times more expensive than AL. Endemic countries throughout Africa have reported with alarm that this severely limits their ability to provide effective antimalarials to their populations and, more broadly, to implement effective malaria control programs, putting lives at risk.

ANSWERING THE CALL FROM PARTNER COUNTRIES

In the context of stagnant funding for malaria control and elimination efforts globally, many countries are being forced to choose between stopping or scaling back other lifesaving malaria interventions in order to buy the more costly ACTs, or to continue to use AL thereby adding to the continuing decline in AL efficacy and poorer patient outcomes. The unfortunate reality is that whether a patient receives an effective malaria treatment today could very well be determined by their country's GDP.

The Gates Foundation, the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund), the U.S. President's Malaria Initiative (PMI), and Unitaid are working with other key stakeholders to take concrete steps to respond to country needs and support the diversification of ACTs, along with other measures to detect and mitigate against antimalarial resistance:

- The Gates Foundation, in partnership with MedAccess and Medicines for Malaria Venture (MMV), are working to lower the cost of ASPY and DP by supporting generic manufacturers and reducing the cost of the key active pharmaceutical ingredients. Additionally, the Gates Foundation is extensively funding development of novel therapeutics to address antimalarial drug resistance in the medium and long term.

- The Global Fund is providing approximately $12 million in Access Funds to several countries with demonstrated commitment to treatment diversification that will subsidize the cost of ASPY and DP. This will increase the amount of ASPY and DP that the Global Fund is able to procure for countries beyond the limited amounts it is procuring through its country grants. Global Fund also funds therapeutic efficacy studies through its regular grant cycle process.

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- PMI funds therapeutic efficacy studies in 25 partner countries in Africa to provide the critical evidence needed to support ACT diversification. Additionally, PMI is procuring ASPY and DP, but currently at limited volumes—approximately 5 million treatments in 2024.

- Unitaid will provide up to $25 million for the design and implementation of a multi-country project providing large-scale product introduction support to accelerate demand and adoption of ASPY, to generate evidence for resistance management strategies like multiple first-line therapies, and to provide resources and expertise to support associated market-shaping activities. The project will support alternative ACT product introduction in 5-7 countries and address knowledge gaps, including feasibility of different multiple first-line therapy approaches.

However, these joint efforts, while critical, are not sufficient to respond to the call from countries and address the immediate needs that countries are facing. Many will take time to bear fruit, while others only cover a small percentage of the need. The cost of newer ACTs is likely to remain higher than AL for at least the next 2-3 years, after which longer term market shaping work will make the products more affordable.

But we cannot afford to wait. Continuing with the status quo not only puts lives at risk, it jeopardizes future antimalarial options, the most promising of which include a lumefantrine component. Introducing these new antimalarials in the context of widespread lumefantrine resistance could threaten the future of important new drug combinations.

OUR COMMITMENT TO FURTHER ACTION

Time is of the essence—we must act to save lives and protect new antimalarial drug options on the horizon. Malaria endemic countries have signaled the need to urgently diversify the ACTs they are using and follow evidence-based policies for antimalarial drug stewardship and resistance management in both the public and private sectors. Modeling demonstrates that delays in diversifying ACTs will result in more treatment failures and likely further the spread of malaria parasites with artemisinin partial resistance, putting millions of lives at risk. Catalytic resources would allow for more timely diversification of ACTs and bring countries' plans and policies to fruition. This critical first step is required both to save lives and avert further acceleration of ACT resistance.

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As funders and champions of malaria control and elimination efforts globally, we are committed to working with partner countries to urgently explore all available options to support diversification of ACTs in countries at high risk of malaria until newer ACTs become more affordable. We call on other donors to join us in this commitment by helping to fill financing gaps and support the immediate procurement of alternative ACTs. In addition to this important first step, we stand ready to support country leadership in establishing long-term, evidence-based policies for antimalarial drug stewardship and resistance management in the public and private sectors.

The global malaria community cannot afford to repeat the deadly delays that previously occurred to address antimalarial resistance. The time to act is now and we are committed to doing so.

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