

Marketing of oral artemisinin-based monotherapy medicines

Background

Plasmodium falciparum malaria has become increasingly resistant to previous first-line treatment therapies, but new combination medicines containing artemisinin derivatives show an over 95% cure rate after a standard short three-day regimen. It is critical that the malaria parasite remains sensitive to artemisinin derivatives. Artemisinin derivatives need to be used in combination with other effective anti-malarial medicines for the treatment of uncomplicated falciparum malaria. However, the widespread practice of using oral artemisinin-based monotherapies, which are easier and cheaper to produce and buy, continues to place an enormous risk of losing artemisinins to parasite resistance. Artemisinins, if used as monotherapy, require to be taken as a full seven-day treatment course in order to completely eliminate the parasite. However, due to the rapid resolution of clinical signs and symptoms, most patients do not complete the required full seven-day treatment, leaving the parasite exposed to sub-therapeutic blood levels, which promotes the development of resistance.

Artemisinin-based combination therapies remain the only medicines for effective treatment of uncomplicated falciparum malaria for several years to come, because alternative treatments are unlikely to enter the market at least until 2015.

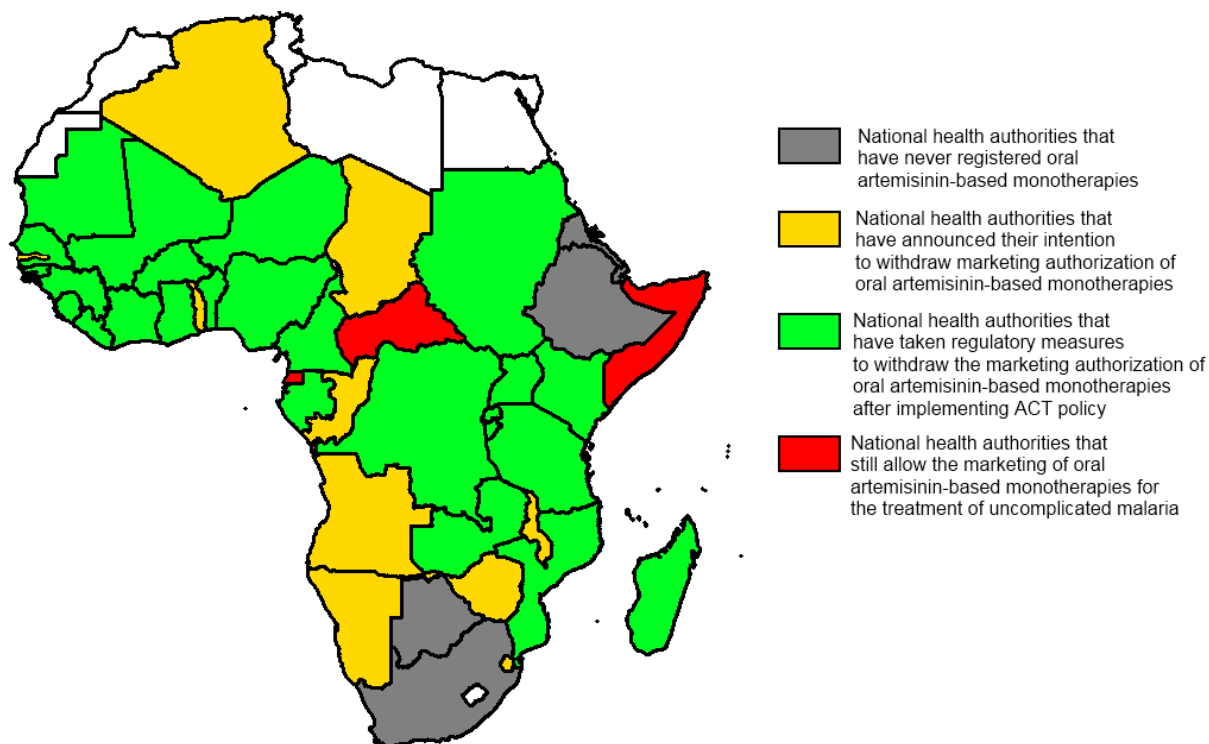
Progress to date

In 2007, the World Health Assembly adopted a resolution to progressively remove oral artemisinin-based monotherapy from the market and instead deploy artemisinin-based combination therapies (ACTs) for the treatment of uncomplicated falciparum malaria. Globally, 35 countries have withdrawn marketing authorization for oral artemisinin-based monotherapy, but 25 countries have not yet taken regulatory action, including 14 in Africa (see map). In 2010 the Roll Back Malaria Partnership (RBM) reaffirmed the commitment to ending the use of monotherapies with Africa's Ministers of Health.

Out of 76 companies involved in the production and marketing of these medicines, a total of 37 companies have de-listed oral artemisinin-based monotherapy from their product catalogues but 39 companies, mainly those targeting the private sector markets of malaria-endemic countries, are still actively providing monotherapy.

Progress made by regulatory authorities at country level shows that phasing out oral artemisinin-based monotherapy from the market is possible through a range of interventions as long as government commitment and strong stewardship of the national regulatory authorities is maintained. A number of successful examples show that phasing out oral artemisinin-based monotherapy can succeed. In Cameroon and Côte d'Ivoire, new regulations have aligned the availability of products for sale in the private sector with those listed in the national treatment guidelines and available in the public sector. Other countries such as Benin have not only removed oral artemisinin-based monotherapy but also all formulations of chloroquine, which is no longer effective. The critical step in Benin was to ensure large-scale availability of ACTs. The examples of India and Pakistan have shown the importance of national regulatory authorities in coordinating this initiative. The active recall of existing stocks of chloroquine and sulfadoxine pyrimethamine in Burundi has proven to be highly effective.

Map outlining marketing situation of oral artemisinin-based monotherapy medicines country level



The way forward: targets for action

Removal of artemisinin-based monotherapy depends on effective drug regulation at country level. Only the removal of marketing authorizations for oral artemisinin-based monotherapies will make them unavailable in the public and formal private sectors. A flourishing informal private sector, which is common in many malaria-endemic countries, will still continue to provide oral artemisinin-based monotherapy to potential users and can be overcome by the provision of good access to quality medicines through a national drug supply management system.

A variety of interventions focusing on both active pharmaceutical ingredients and finished pharmaceutical products can and have successfully been applied to interrupt the manufacture and sale of oral artemisinin-based monotherapies:

- Export markets can be influenced by regulatory actions targeting countries which are the major exporters of these medicines. In particular, withdrawing manufacturing and export licenses can

prevent pharmaceutical companies from exporting their oral artemisinin-based monotherapy products to malaria-endemic countries.

- To protect domestic markets, the most effective strategy is to stop import licenses and to not grant marketing authorizations for such products. Domestic manufacturers should be regulated more stringently with regard to import licenses.
- In addition, to regulate domestic companies involved in the re-packaging or re-branding of artemisinin monotherapies, import licenses should be suspended for companies exclusively marketing oral artemisinin-based monotherapies.
- It is crucial to ensure large-scale availability of ACTs in both the public and private sectors, before oral artemisinin-based monotherapies can effectively be removed from the market.

Key steps at country level

- Agreement on timeframe for phasing out oral artemisinin-based monotherapies in synchrony with immediate large-scale implementation of artemisinin-based combination therapies (ACTs).
- Suspension of new approvals of marketing authorizations for oral artemisinin-based monotherapies.
- Suspension of import licenses for artemisinin or its derivatives to domestic companies exclusively marketing oral artemisinin-based monotherapies.
- Large-scale deployment of ACTs in the public sector and communication to prescribers and consumers to move away from monotherapies.
- Widespread availability and affordability of ACTs in the private sector.
- Withdrawal of marketing authorization and of manufacturing licenses for oral artemisinin-based monotherapies.
- Suspension of export license for oral artemisinin based monotherapies.
- Active recall of oral artemisinin-monotherapies from the market.
- Complete elimination of oral artemisinin-based monotherapy medicines from the market.

ALMA next steps

In partnership with WHO and RBM, ALMA urges that all ALMA countries ensure that regulatory measures to stop marketing of oral artemisinin-based monotherapies and to promote access to artemisinin-based combination therapies (ACTs) are in place by end 2010.

Background reading

- Regulatory action needed to stop the sale of oral artemisinin-based monotherapy. WHO Drug Information Vol. 24, No. 2, 2010.
http://www.who.int/malaria/generic_guide_regulatory_action.pdf
- World Health Assembly Resolution WHA 60.18.
http://apps.who.int/gb/ebwha/pdf_files/WHA60/A60_R18-en.pdf

More comprehensive information on oral artemisinin-based monotherapy can be obtained on the webpage of the WHO Global Malaria Programme:

http://www.who.int/malaria/marketing_of_oral_artemisinin_monotherapies/en/index.html