Threat of oral artemisinin-based monotherapies

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World Health Organization
Slow progress....

Companies marketing oral artemisinin-based monotherapies by year of identification by WHO

37/76 (49%) companies withdrew their products
39/76 (51%) not yet in line with WHO recommendations
(last updated 14.09.2010)

Number of companies

<table>
<thead>
<tr>
<th>Year</th>
<th>Not yet contacted</th>
<th>Withdrawn monotherapies</th>
<th>Intention to comply</th>
<th>No intention disclosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td></td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>5</td>
<td>10</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>2007</td>
<td>15</td>
<td></td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>2008</td>
<td>10</td>
<td></td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>2009</td>
<td>5</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>2010</td>
<td>5</td>
<td></td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>

Last updated on 26.04.20
Manufacturing sites/place of registration of producers of oral artemisinin monotherapies
Slow progress...

National Drug Regulatory Authorities:
28/78 (36%) still allow oral monotherapies
Last updated on 26.04.2010

Risk of development of resistance

Number of countries still allowing monotherapies
28 countries allow the marketing of oral artemisinin-based monotherapies: 17 in Africa

Algeria, Angola, Bangladesh, Bhutan, Bolivia, Botswana, Cape Verde, Central African Republic, Chad, Colombia, Congo, Equatorial Guinea, Gambia, Malawi, Myanmar, Namibia, Nepal, Papua New Guinea, Sao Tome & Principe, Solomon Islands, Somalia, Swaziland, Timor Leste, Togo, Vanuatu, Zambia, Zimbabwe and Yemen
Public Sector Availability of Antimalarials

<table>
<thead>
<tr>
<th>Country</th>
<th>First Line Treatment</th>
<th>Non-Artemisinin Monotherapy</th>
<th>Oral Artemisinin Monotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benin</td>
<td>90</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Cambodia</td>
<td>60</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>DRC</td>
<td>50</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Madagascar</td>
<td>70</td>
<td>35</td>
<td>15</td>
</tr>
<tr>
<td>Nigeria</td>
<td>80</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Uganda</td>
<td>90</td>
<td>80</td>
<td>10</td>
</tr>
<tr>
<td>Zambia</td>
<td>70</td>
<td>45</td>
<td>5</td>
</tr>
</tbody>
</table>
Private Sector Availability of Antimalarials

![Chart showing availability of antimalarials in various countries.](chart.png)

- **First Line Treatment**
- **Non-Artemisinin Monotherapy**
- **Oral Artemisinin Monotherapy**
Relative Volumes of Antimalarials Distributed by Sector and Drug Type

![Graph showing relative volumes of antimalarials distributed by sector and drug type for different countries. The graph includes bars for public and private sectors, and different colored sections within each bar indicate the percentage of first line ACTs, other ACTs, non-artemisinin monotherapies, and oral artemisinin monotherapies.](image)
Main challenges

- A number of companies do not respond to WHO appeal
- Most of "non-responders" market oral artemisinin monotherapies
- Poorly regulated pharmaceutical market in endemic countries
- Limited access to ACT: i) slow roll-out of ACTs in the public sector and ii) limited penetration of ACTs in the private sector
- Manufacturing of sub-standard products exploiting "niche market" left open by companies complying to WHO recommendations
- Need of multiple sources of information for monitoring
Phasing out chloroquine and SP in Burundi

- 2001 - efficacy studies comparing AS+AQ vs AL to evaluate potential alternatives to CQ (1st-line) and SP (2nd-line) for malaria treatment
- July 2003 – adoption of AS + AQ as 1st-line treatment based on study results
- November 2003 - introduction of the new medicine and MOH regulation (ordonnance) to remove CQ and SP from the market. Measures included:
  - stopping importation of CQ and SP,
  - active recall of CQ and SP from all public health facilities and Provincial warehouses
  - immediate stop of in-country distribution of CQ and SP stocks available at central level by the Centrale d'Achat des Médicaments Essentiels du Burundi (CAMEBU) and donation of these stocks to neighbouring countries still deploying these medicines, and
  - sales ban of CQ and SP products in the private sector.
- In 2008 the DNDi survey on ACT implementation in Burundi confirmed the complete absence of CQ and SP in both public and private sector health facilities, warehouses and pharmacies across the country.
Artemisinin Conference 13 October 2010

Decision of Cameroon in May 2006

Including rectal artesunate recommended by WHO for pre-referral treatment of severe malaria in children

GLOBAL MALARIA PROGRAMME

42 médicaments du paludisme interets

Depuis quelques années, de nombreux médicaments sont déclarés inaptes à la guérison du paludisme.

Including rectal artesunate recommended by WHO for pre-referral treatment of severe malaria in children

GLOBAL MALARIA PROGRAMME

World Health Organization
Decision of Cambodia in March 2009

Withdrawal of Marketing Authorization of oral artemisinin-based antimalarial medicines

- widespread dissemination of new regulation (posters + leaflets)
- empowerment of drug inspections (confiscation, fines, prosecution)
- letters of appreciation + logos for approved outlet
Withdrawal of Marketing Authorization of 22 brands of chloroquine and of 24 brands of oral artemisinin-based monotherapies
### Liste des molécules et combinaisons de molécules antipaludiques non recommandées par le nouveau schema thérapeutique

- ARTESUNATE 200 mg (forme supposoire, Adulte) = PLASMOTRIM
- ARTESUNATE/MEFLOQUINE = ARTEQUIN
- ARTESUNATE/NAPHTOQUINE = ARCO
- ARTESUNATE/SULFAMETHOXYPYRAZTNE/PYRIMETHAMINE = CQ-ARINATE
- ARTESUNATE/SULFADOXINE/PYRIMETHAMINE = ARTEDAR 50 et 100 mg
- DIHYDROARTEMISININE/PIPERAQUINE/DUO-COTECXIN, MALACUR, DARTE-Q
- DIHYDROARTEMISININE/PIPERAQUINE/TRIMETHOPRIME = ARTECOM
- AMODIAQUINE/SULFAMETHOXYPYRAZINE = DUALKIN

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**Decision of the Côte d'Ivoire in August 2009**

The withdrawal of certain ACTs from the market to align the private sector with the public sector.
Consultation with Swissmedic (30.3.10):

- The company NYD has an authorisation from Swissmedic for the "Trade of medicinal products in foreign countries". Since these products are not manufactured in Switzerland and do not transit Swiss territory, they don't need market authorisation from Swissmedic.

- Article 21 al. 1 of the LPT stipulates that the export of medicinal products and their foreign trade from Switzerland shall be prohibited if:
  - a. they are prohibited in the destination country;
  - b. circumstances suggest that they could be intended for an illegal purpose.

- Since neither a) or b) apply, the Swiss law does not allow any intervention.
Phasing out oral artemisinin-based monotherapies

A. annua seed producers/distributors

Artemisinin extractors/growers

API suppliers of artemisinin derivatives

Manufacturers of quality ACTs

Manufacturers of substandard ACTs

Manufacturers of oral artemisinin monotherapies

Export

Domestic market

Export

Export

National Regulatory Authority (NRA) of recipient countries

Market intelligence (surveys of quality of medicines)
Progress and next steps

1. Follow-up of 2nd African Medicines Regulators Conference (24-26 Nov 2009, Maputo, Mozambique)
   a. Meeting with African NRAs (Francophone - Douala, 28-30 June 2010)
   b. Meeting with African NRAs (Anglophone - Dar Es Salaam, 8-9 Nov 2010)

2. WHO/AFRO Regional Committee (RC 59) Resolutions on Acceleration of Malaria Control towards elimination and Monitoring Drug resistance related to Malaria, Tuberculosis and HIV

3. Presentation to Ministerial Session at RBM Board, 14 May 2010

4. Presentation African Leaders Malaria Alliance (ALMA) – July 2010
