Pediatric treatments for malaria.
Experiences from Africa and other regions

David Reddy PhD
CEO, MMV
A child dies (needlessly) from malaria every 2 minutes

• Between 2010 and 2016, at least 2.0 million children died from malaria¹.

• While the number of paediatric deaths dropped by 35% during this time period, 285,000 children under 5 years of age still died from malaria in 2016 – an unacceptable number².

• Children who survive severe malaria may have to cope with life-long consequences: “neurological and cognitive impairments associated with severe or cerebral malaria have been reported in numerous studies”³.

¹ WHO World Malaria Report 2017; http://www.who.int/features/factfiles/malaria/en/ reports at least 70% of malaria deaths are in children under 5
² http://www.who.int/en/news-room/fact-sheets/detail/malaria
https://doi.org/10.1016/S0140-6736(07)60076-2
Malaria medicines for children: focusing foremost on those most at risk

• In 2007, the World Health Assembly issued a key resolution for Better Medicines for Children.

• In 2009, WHO developed its first Essential Medicines List for children, 32 years after the creation of the original list – an acknowledgement that children are not “mini-adults” to be treated with fractionated doses of adult tablets.

• The Better Medicines for Children campaign promoted child-friendly medicines that meet dosing, tolerability, and ease-of-administration requirements.
Until 2009, treating children with malaria was a nightmarish struggle

• The 2009 Essential Medicines List for children (2nd ed.) for the first time included a dispersible artemisinin-based combination therapy (ACT).

• The 3rd edition of the List in 2011 added a second ACT – but its water-soluble presentation was not yet flavor-masked.

The daunting challenge of dosing children with bitter tablets in late 2008
Vast majority of private drug shops continued to sell questionnable products for children

Source: F. Camus-Bablon 2012
MMV-supported projects in 2000

Research
- Lead optimization
- Candidate profiling

Translational
- Preclinical
- Human volunteers
- Patient exploratory

Product development
- Patient confirmatory
- Regulatory review

Access
- Approved/ERP

Cystein protease inhibition
Synthetic peroxide
MMV-supported projects in April 2018

MMV support to projects may include financial, in-kind, and advisory activities.

Footnotes:  🌐 Included in MMV portfolio after product approval and/or development. DNDi and partners completed development and registration of ASMQ and ASAQ. 🌐 Global Fund Expert Review Panel (ERP) reviewed product – permitted for time-limited procurement, while regulatory/WHO prequalification review is ongoing. ✨ WHO Prequalified OR approved/positive opinion by regulatory bodies who are ICH members/observers. 🚿 Paediatric formulation. ⭐ For children 13 – 60 months; ⭐⭐ For infants 3 – 12 months.

Brand names 1: Coartem® Dispersible; 2: Artesun®; 3: Eurartesim®; 4: Pyramax® tablets or granules; 5: ASAQ Winthrop®; 6: SPAQ-COTM

April 2018
WHO’s Essential Medicines List for children includes now five ACTs from MMV and partners

The call of Better Medicines for Children is being answered… quality options have increased dramatically over the last five years.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AL Dispersible (innovator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic versions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PYAS Granules (innovator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>ASAQ (innovator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>Generic versions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>DHA-PQP (innovator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2013</td>
<td>2014</td>
<td>2015</td>
<td>2017</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASMQ (innovator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2017</td>
<td></td>
</tr>
</tbody>
</table>

Child-friendly formulation: disperseable or granules

Dosing possible >5kg: formulation not ideally suited for pediatric dosing

A-L: artemether/lumefantrine; PYAS: pyronaridine/artesunate; ASAQ: artesunate/amodiaquine; DHA-PQP: dihydroartemisinin/piperaquine; ASMQ: artesunate/mefloquine
Timeline depicts first of either stringent regulatory or WHO Prequalification approvals.
Key: E58: EMA Article 58; EMA; EMA Marketing Authorization; SM: Swissmedic; PQ: WHO Prequalification
MMV-supported products have had significant impact and saved an estimated >1.5 million lives since 2009

350 million treatment courses\(^1\) delivered by Novartis to over 50 countries

**Saving an estimated >875,000 children lives**

>100 million vials of Artesun delivered since 2011\(^2\)

**Saving an estimated 650,000 additional lives\(^3\)**

Reducing uncomplicated and severe malaria episodes by 75\%\(^4,5\)

**Protecting 19 million children**

Available starting in 2017, with 460,000 treatments delivered in 2017

**Halving disability and death of children with severe malaria\(^6\)**

---

1 Source – Novartis press release 2017
2 Source – Fosun 2017
3 Additional childrens lives saved by providing injected artesunate versus injected quinine to children with severe malaria – AQUAMAT and SEAQUAMAT studies
4 WHO
5 Gulin distribution data (2017)
6 WHO TDR Study 13
How can we ensure that we maintain the gains in treating children with malaria?

• **Drug Developers:** stay focused on children as a key patient target for new malaria medicines.

• **Procurement Partners:** embrace the prioritization of Better Medicines for Children whenever possible.

• **Practitioners:** get access and use quality medicines for children and be trained in the dosing requirements and treatment protocols for children.

• **Public health guidance:** include quality medicines for children that have been developed to international regulatory standards (quality, safety and efficacy) in national essential medicines lists and recommend them for use in malaria endemic countries.