ASMQ FDC a simple and child-friendly ACT developed for Asia and Latin America

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DNDi
Drugs for Neglected Diseases initiative
Iniciativa Medicamentos para Enfermedades Olvidadas
AS-MQ used over 19 years since 1992 in 3 continents, Clinical data reported from more than 36,000 patients, 81 studies in 20 countries
The Blueprint of ASMQ Tablet

- Quality components (AS, MQ, excipients)
- Smallest possible size (Minimum excipients)
- Good aspect (Coating)
- Paediatric strengths; rapid disintegration in water
- Simple (1 or 2 tablets for 3 days)
- Stable (Process and Tropical conditions)
- Adequate biopharmaceutical properties
Predicted and Measured Profiles for MQ in Adult Patients (Thailand)

- **FDC**: 8mg/kg/d x3d
- **non-Fix**: MQ15+10MKD at 24,48H as loose combination with AS

28 days
# ASMQ FDC: pragmatic dosing regimen

## Recommended Dosage for ASMQ FDC Tablets

<table>
<thead>
<tr>
<th>Asia</th>
<th>Latin America</th>
<th>Recommended Dose, daily for 3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (Kg)</td>
<td>Age</td>
<td>Weight (Kg)</td>
</tr>
<tr>
<td>5 – 8</td>
<td>6 -11 months</td>
<td>5 – 8</td>
</tr>
<tr>
<td>9 – 17</td>
<td>1 – 6 years</td>
<td>9 – 17</td>
</tr>
<tr>
<td>18 – 29</td>
<td>7 – 12 years</td>
<td>18 – 29</td>
</tr>
<tr>
<td>≥ 30</td>
<td>≥ 13 years</td>
<td>≥ 30</td>
</tr>
</tbody>
</table>

<sup>1</sup>Mefloquine HCl 55 mg are equivalent to 50 mg of mefloquine

<sup>2</sup>Mefloquine HCl 220 mg are equivalent to 200 mg of mefloquine
ASMQ
Small Tablets-Paediatric Strengths & Easy to use

ASMQ FDC is easy to use as 1, 2, 3!

1 dose 2 products 3 days
One single daily dose of 1 or 2 tablets of two highly effective combined products for three days of affordable medicine

INFANT DOSE < 1 YEAR

NEW FACT ASMQ

AS: 100mg
MQ(salt): 220mg

Once a day

Day 1

Day 2

Day 3

NON-FIXED AS and MQ

AS: 50mg
MQ(salt): 250mg

Once a day
ASMQ FDC, Key studies performed and ongoing

Thailand
N=24, Ph.1-HNV
PK & Tolerability
N=50, Ph.2
PK, efficacy & safety
N=50, Ph.2b
PK, efficacy & safety
N=500, Ph.3
Efficacy & safety

Myanmar, Ph.4
N=808
Comparative Effectiveness

India Ph.3
N=77
PK, efficacy & safety

Brazil, Intervention Study
Ph. 3b/4
N=23,760

Ongoing studies

Performed studies
ASMQ in Brazil

• **Phase IIIb/IV, intervention study** to evaluate the impact of programmatic use of ASMQ FDC in Acre and Pará (Amazon Basin) in comparison with standard regimen used in Brazil (MOH/PAHO/RAVREDA)

• **23.760 patients (including 8.880 children)** treated between 2006 and 2008

**Safety**

✓ No malaria deaths reported during the study period
✓ No serious adverse events reported
✓ No direct reports to the free-toll PV number from Farmanguinhos
✓ No reports to the national regulatory agency, ANVISA
Effect of the artesunate mefloquine fixed dose combination in the malaria transmission in Amazon basin communities

Incidence rate of malaria

Ratio P. falciparum/P. vivax

Hospital admissions due to malaria
ASMQ FDC in Amazon Basin, subset analysis

Proportion of slides with asexual falciparum parasitaemia until D40 post-ASMQ treatment in Cruzeiro do Sul, stratified by age

<table>
<thead>
<tr>
<th>Total patients</th>
<th>&lt; 1 year</th>
<th>1 - 6 years</th>
<th>7 - 13 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/584</td>
<td>0/6</td>
<td>1/267</td>
<td>2/311</td>
</tr>
<tr>
<td>(0.5%)</td>
<td>(0)</td>
<td>(0.37%)</td>
<td>(0.64%)</td>
</tr>
</tbody>
</table>
Comparing the effectiveness of 5 artemisinin combination treatment regimen in Myanmar

Comparative efficacy

Cumulative proportion of patients with vivax malaria during follow-up
ASMQ in children: Evaluation of *P. falciparum* recrudescence rate at D63 by PCR in Myanmar

![Graph showing the number of patients in different age groups with different treatment outcomes.](image)

- N = 423
- 5-14 y.o. = 298
- < 5 y.o. = 87
ASMQ in INDIA

• **Phase III study** to assess efficacy, safety and PK of ASMQ FDC in 77 adults with uncomplicated *falciparum* malaria in Goa & Mangalore (ICMR-India)

• **Efficacy** results after PCR correction: 100% at Day 63

• **Safety & tolerability** assessment: 3.9% drug related AEs
  No drug discontinuation related to AE

• **Pop. PK:** model developed based on
  sparse sampling (AS/DHA/MQ)
  DHA equivalents  $t_{1/2}$ : 2.08 Hrs
  Cmax : 1500 ng/ml
  MQ  $t_{1/2}$ : 21.6 days
ASMQ in AFRICA

- **Phase IV study** to compare the efficacy and safety of ASMQ fixed-dose combination vs. AL in 940 children under 5 y.o. with uncomplicated *falciparum* malaria

- **Countries**: Burkina Faso (CNRFP), Kenya (KEMRI) and Tanzania (NIMR)

- Supervised 3 days treatment in hospital
- Efficacy trial (cured at D63)
- Safety and tolerability
- Population PK of AS, MQ and Lumefantrine
Progress/ Project Timelines

- Inclusions curve:

  - First patient inclusion: in Q4 2010
  - Last Patient inclusion: Planned in Q2 2012
  - Last visit of the last patient: Planned in Q3 2012
  - Results: Planned in Q4 2012/Q1 2013
ASMQ: Advances & Challenges
From Brazil to Asia and Africa

• Registered by Farmanguinhos in Brazil in 2008 and implemented by the Brazilian national programme
• Donations to Bolivia and negotiations in Peru and Venezuela
• Successful technology transfer to Cipla (India)
• Cipla filing to WHO pre-qualification and Indian/ASEAN registration
• Positioning ASMQ
  • Clinical studies completed: Latin America (Brazil), Asia (India, Myanmar)
  • Clinical studies on going: Africa (Tanzania, Burkina Faso, Kenya), Asia (Malaysia)