THE GROWING MARKET FOR AMOXICILLIN DISPERSIBLE TABLETS

Opportunity Assessment for Potential Manufacturers
Copenhagen, Denmark
September 23, 2014
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1. Overview/background
2. Market size and demand
3. Market trends
Pneumonia is the number one killer of children under five. Most demand resides in Africa and SE Asia.

Notes: 1) Child Survival Call to Action, Ending Preventable Child Deaths Summary Roadmap Version 1, June 14, 2012
Global momentum and support for ending preventable deaths from childhood pneumonia

Recent events highlighting global focus:

UN Commission on Life Saving Commodities
Global coordinated effort to scale up priority commodities, including Amoxicillin DT

WHO/UNICEF: Ending preventable child deaths from pneumonia and diarrhoea by 2025
The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)

Lancet Series on Childhood Pneumonia and Diarrhoea launched on April 12, 2013
Lancet series focused on opportunities in treating childhood pneumonia

Just a few of the partners with ongoing global support for scale-up of Amoxicillin DT:
WHO and others continue to support global advocacy around the use of Amoxicillin DT

Significant advocacy work is well underway around pneumonia treatment:

www.worldpneumoniaday.org

Coming Soon
Revised WHO classification and treatment of pneumonia in children at health facilities:

- Advocacy Brief
- Policy Brief
- Evidence Summary
Rapid scale up of quality, affordable, and dependable supply of Amoxicillin DT is needed

97M$^1$ cases of childhood pneumonia annually $\rightarrow$ 1.1M$^2$ children die annually $\rightarrow$ WHO defines the optimal treatment as Amoxicillin DT $\rightarrow$ Need for supply to grow rapidly in the coming years

- Most cases occur in just 10 low and middle income countries
- Estimates show as many as 80% of all children go untreated or incorrectly treated with antibiotics
- Most common antibiotic in use is Cotrimoxazole
- Many cases are undiagnosed or incorrectly diagnosed
- Pneumonia is the number one killer of children under five

WHO defines the optimal treatment as child friendly amoxicillin in 250mg dispersible tablets (DT)

- Technical guidance from the WHO has defined the optimal treatment as child friendly amoxicillin in 250mg dispersible tablets (DT)
- To meet this growing demand, new quality manufacturers are needed
- Requirements:
  - Speed to scale-up
  - High quality
  - Price
  - Supply security

The need:
Amoxicillin Dispersible Tablets (DT) 250mg

The benefit:
- Child friendly, simple dosing, effective
- No cold-chain requirement

WHO recommends treating childhood pneumonia with Amoxicillin. Dispersible tablets are the optimal formulation.

### WHO’s New Pneumonia Treatment Guidelines for Case Management

<table>
<thead>
<tr>
<th>Age</th>
<th>Pneumonia in low HIV prevalence areas</th>
<th>Pneumonia in high HIV prevalence areas</th>
<th>Severe pneumonia</th>
<th>Severe pneumonia with danger signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 months</td>
<td>1st dose antibiotic, referral to health facility for supportive therapy</td>
<td>1st dose antibiotic, referral to health facility for supportive therapy</td>
<td>1st dose antibiotic, referral to health facility for supportive therapy</td>
<td></td>
</tr>
<tr>
<td>2 – 12 months</td>
<td>1 Amoxicillin 250mg tablet / twice a day / 3 days</td>
<td>1 Amoxicillin 250mg tablet / twice a day / 5 days</td>
<td>1 Amoxicillin 250mg tablet / twice a day / 5 days</td>
<td>1st dose antibiotic, referral to health facility for supportive therapy</td>
</tr>
<tr>
<td>12 – 59 months</td>
<td>2 Amoxicillin 250mg tablets / twice a day / 3 days</td>
<td>2 Amoxicillin 250mg tablets / twice a day / 5 days</td>
<td>2 Amoxicillin 250mg tablets / twice a day / 5 days</td>
<td>1st dose antibiotic, referral to health facility for supportive therapy</td>
</tr>
</tbody>
</table>

### Dispersible Tablet Benefits

- Cheaper than its equivalent oral suspension
- Facilitates and simplifies Community Case Management (CCM) and greater dosage accuracy compared to OS (which has to be manually measured and mixed)
- No refrigeration/cold-chain needed
- Come in appropriate strengths and pack sizes to meet the needs of CHWs, caregivers, and children
- Are packaged for easy dispensing and inventory management—course of treatment is one or multiple blister strips and light weight
- Do not have to be split to get the correct dosage

Notes:
1) Qazi, Shamim, Management for Pneumonia in Developing Countries, WHO, Geneva, June 2013.
The global health community is facilitating scale up of Amoxicillin DT by addressing all bottlenecks

**The Treatment Process**

**Trigger / Information Gathering**
- Mother contacts CHW/Pharmacist
- Mother unaware and does nothing

**Assessment**
- Timer, etc (fever + fast breathing)
- Visual and verbal diagnosis
- RDT blood test
- Child not there – mother describes

**Classification**
- Severe pneumonia
- Less severe pneumonia
- Malaria

**Management**
- Antibiotics
- Anti-malarials
- Oxygen
- Inject. antibiotics
- Anti-fever meds
- Nothing (get rest and feed)

**Antibiotics Choice**
- Amoxicillin DT (250mg)
- Amoxicillin (other formulations)
- Cotrimoxizole
- Other non-optimal (Cipro, etc.)

**Leverage Points being addressed by the global health community**

1. **Trigger/Information Gathering**: 
   - Demand generation campaigns to raise awareness of signs of pneumonia and importance of seeking care

2. **Evaluation and Diagnosis**: 
   - Training and education for caregivers
   - New diagnostic technologies and protocols being developed

3. **Treatment Options**: 
   - WHO recommends Amoxicillin DT
   - Global advocacy for inclusion on countries’ Essential Medicine Lists and Standard Treatment Guidelines

4. **Amoxicillin choice**: 
   - WHO recommends Amoxicillin DT
   - Global advocacy for inclusion on countries’ Essential Medicine Lists and Standard Treatment Guidelines
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Up to 71 million cases of suspected childhood pneumonia may not currently receive antibiotics

Suspected childhood pneumonia cases in 50 low/middle income countries\(^1\) (2014 – 2020)

*Note: Treatment rates estimated using a combination of the latest DHS, MICS or NFHS data – depending on what was available for each country. In some cases, like India, antibiotic usage may be higher and the size of the “untreated” population may be an overestimate.

Notes:  
1) Estimates by John Snow, Inc for the 49 Every Woman, Every Child countries + India  
2) Updated August 2014 with 2010 CHERG estimates of incidence of clinical pneumonia (published 2013) - Using latest DHS/MICS estimates of those children 5 and under receiving antibiotics for treatment of ARI
10 focus countries account for 77% of all untreated suspected childhood pneumonia cases

Pareto of childhood pneumonia in 50 low/middle income countries (2014)
Total = 97M cases

Notes: 1) Estimates by John Snow, Inc for the 49 Every Woman, Every Child countries + India
2) Updated August 2014 with 2010 CHERG estimates of incidence of clinical pneumonia (published 2013) - Using latest DHS/MICS estimates of those children 5 and under receiving antibiotics for treatment of ARI
The 10 focus countries for global scale-up of Amoxicillin DT have strong demand growth.

Potential childhood pneumonia Amox DT demand in 10 focus countries\(^1,2,3,4,5\) (2014 – 2018)

<table>
<thead>
<tr>
<th>Year</th>
<th>India</th>
<th>Pakistan</th>
<th>Bangladesh</th>
<th>Nigeria</th>
<th>DRC</th>
<th>Uganda</th>
<th>Kenya</th>
<th>Tanzania</th>
<th>Afghanistan</th>
<th>Ethiopia</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>384</td>
<td>74.8</td>
<td>37.3</td>
<td>35.1</td>
<td>19.2</td>
<td>18.9</td>
<td>14.6</td>
<td>13.5</td>
<td>6.2</td>
<td>5.9</td>
</tr>
<tr>
<td>2015</td>
<td>392</td>
<td>76.2</td>
<td>38.2</td>
<td>36.0</td>
<td>19.8</td>
<td>19.4</td>
<td>15.0</td>
<td>13.9</td>
<td>6.3</td>
<td>6.9</td>
</tr>
<tr>
<td>2016</td>
<td>399</td>
<td>77.6</td>
<td>39.2</td>
<td>37.0</td>
<td>20.5</td>
<td>19.9</td>
<td>15.5</td>
<td>14.3</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>2017</td>
<td>407</td>
<td>72.4</td>
<td>40.2</td>
<td>38.0</td>
<td>21.1</td>
<td>20.5</td>
<td>16.0</td>
<td>14.7</td>
<td>7.5</td>
<td>7.7</td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td>73.2</td>
<td>41.2</td>
<td>39.0</td>
<td>21.8</td>
<td>21.0</td>
<td>16.4</td>
<td>15.1</td>
<td>7.7</td>
<td></td>
</tr>
</tbody>
</table>

5-year total demand in 10 focus countries: \(~2B\) tablets\(^5\)

Notes:
1) Estimates by John Snow, Inc
2) Countries included: India, Nigeria, DRC, Pakistan, Ethiopia, Tanzania, Uganda, Bangladesh, Kenya, Niger
3) Scale up scenario increases base year (2013) coverage by population growth and 3% annual increase in treatment coverage to 2017
4) Low treatment coverage estimates for India (13%) likely underestimate treatment figures
5) Assumes 20 tablets per course; this over-estimates for children under age 1 who require 10 tablets, likely off-set by use for other conditions
Orders for Amoxicillin DT through UNICEF have seen strong growth

UNICEF Procurement:
Amoxicillin DT and Amoxicillin Oral Suspension (number of treatments)

CAGR = 128%
All high-burden countries either already have, or are in process of updating national guidelines to Amox DT.

- Bangladesh: Yes
- DRC: In progress
- Niger: In progress
- Pakistan: In progress
- Tanzania: In progress
- Uganda: In progress
- Ethiopia: In progress
- India: In progress
- Kenya: In progress
- Nigeria: In progress
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Economic growth in developing countries is increasing demand for pharmaceutical products.

Global Pharmaceutical Market (2010)\(^1,2\)

Value and Growth Rate by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>2010 Market Size ($B)</th>
<th>Compound Annual Growth Rate (CAGR, 2010 – 2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>$335.0</td>
<td>4%</td>
</tr>
<tr>
<td>Europe</td>
<td>$245.0</td>
<td>4%</td>
</tr>
<tr>
<td>Japan</td>
<td>$97.0</td>
<td>5%</td>
</tr>
<tr>
<td>Asia/Pacific</td>
<td>$113.0</td>
<td>9%</td>
</tr>
<tr>
<td>South America</td>
<td>$53.0</td>
<td>9%</td>
</tr>
<tr>
<td>Africa</td>
<td>$15.0</td>
<td>9%</td>
</tr>
</tbody>
</table>

Notes: 1) “Market Report: World Medical Device Market,” Acmite Market Intelligence
2) IMS via Investment Fund for Health in Africa
4) World Bank, Data Bank (data.worldbank.org)

Demand growth in Africa for healthcare commodities will be among the strongest in the world in the next decade.

Pharmaceutical spending in Africa expected to reach $30B by 2016 and $45B by 2020\(^3\).

Per capita healthcare spending increase for the decade ending in 2011\(^4\):

+225% In Africa

+173% In South Asia
Additional areas of growth for amoxicillin will keep the market strong

<table>
<thead>
<tr>
<th>Market Trend</th>
<th>Implication for Amoxicillin global market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccines for pneumonia</td>
<td>• Many pneumonia vaccines are in testing and are currently being rolled out. While they will certainly have an impact on the prevalence of pneumonia, they are still in their early stages of use and a need for treatment will remain.</td>
</tr>
<tr>
<td>Difficult diagnosis</td>
<td>• Many organizations and multi-national medical technology companies are actively developing and testing new diagnostic tools for childhood pneumonia. New successful innovations will likely increase the demand for amoxicillin treatment.</td>
</tr>
<tr>
<td>Competition from competitive products</td>
<td>• Competition from alternative products remains, including cotrimoxizole. The WHO, however, recommends amoxicillin as the first line and secondary response to cases of pneumonia and severe pneumonia.</td>
</tr>
<tr>
<td>New research in malnutrition treatment</td>
<td>• New research(^1) shows the potential benefits for integrating antibiotics (including amoxicillin) into fighting severe childhood malnutrition. This would likely further increase the size of the Amoxicillin market.</td>
</tr>
<tr>
<td>Treatment of newborn sepsis</td>
<td>• Amoxicillin DT is a growing secondary treatment choice for newborn sepsis. This would likely further increase the size of the Amoxicillin market.</td>
</tr>
</tbody>
</table>

Notes:  
R4D has successfully applied market dynamics strategies to improve access to various life-saving commodities

**R4D’s Market Dynamics team**

- Focuses on increasing global access to high-quality and affordable life-saving products for the poor.
- The team has more than three decades of collective experience working with stakeholders across the global value chain – manufacturers, major donors, and country level stakeholders – to develop and shape markets for health, nutrition, and sanitation in Africa, Asia, and Latin America.

**Results for Development**

- **Malaria bed net market**: Drove strategies to save $600M to protect 300M additional people
- **HIV/AIDS drugs**: Designed Market-shaping Strategy to save $520M on AIDS drugs
- **Neglected diseases**: Actively worked with suppliers to support a 10x drug production increase
- **Global malaria diagnostic market**: Potentially increase impact delivered from donor allocated funds by 400%
- **Global micronutrient market**: Strategies can reach 34M low-income children who require access to critical nutrition products.
- **Lifesaving products for women and children**: Partnered with UN Commission on global market strategies to save millions of lives
R4D’s Market Dynamics team is launching a 3-year BMGF-funded project to scale up access to amox DT

Project goal: Identify and address barriers preventing the scale-up of amox DT

**Supplier-level**
- Share global forecasts with grounding in country-level data
- Assist suppliers in prioritizing key market actions – e.g. Increases in capacity depending on market needs
- Provide market transparency – e.g. tender calendars for high-volume markets – to assist manufacturers in efficient operations
- Help secure effective, affordable, and sufficient supply of amoxicillin DT

**Country-level**
- Gather amox DT demand forecasting and procurement volumes and pricing data across high-burden countries
- Support increased public sector amox DT volumes and access in one focus geography and two lighter touch geographies
- Serve as national champion in key geographies – including amox DT registration, inclusion in guidelines, securing of financing, and procurement.

**Global-level**
- Support resource mobilization for amox DT
- Help develop strategies with donors which incorporate private sector scale-up
Both USAID and the Bill & Melinda Gates Foundation are actively supporting the scale-up of Amoxicillin DT

“USAID is committed to scaling up the use of Amoxicillin DT for the treatment of childhood pneumonia – the number 1 killer of children under-five – in our effort to end preventable maternal and child deaths.”

- David Milestone, USAID

“Increasing the availability of Amoxicillin DT and ensuring its widespread use as the first line treatment for childhood pneumonia is the cornerstone of the Pneumonia team’s treatment strategy”

- Rasa Izadnegahdar, Bill & Melinda Gates Foundation
Resources

This information was prepared by:

- USAID, Center for Accelerating Innovation and Impact
- Results for Development Institute
- UNICEF and UNICEF Supply Division
- Bill & Melinda Gates Foundation

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- David Muhia, UNICEF Supply Division – dmuhia@unicef.org

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