Key Issues in Planning for Procurement of New Pediatric TB Formulations

Shelly Malhotra
Director, Market Access
Shelly.malhotra@tballiance.org

March 2, 2015
Today’s Treatment Situation for Children with TB

NO appropriately-dosed, easy-to-administer, first-line TB drugs for children globally available

Adult treatments are often cut or crushed to achieve desired dose

Gap of 7 years or more projected between launch of adult treatments and availability of child formulations
WHO Dosing Guideline Change for Children in 2010

Source: WHO Child TB Guidelines, 2014

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Range (mg/kg)</th>
<th>Maximum Dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>isoniazid (H)</td>
<td>10 mg/kg (range 7–15 mg/kg)</td>
<td>maximum dose 300 mg/day</td>
</tr>
<tr>
<td>rifampicin (R)</td>
<td>15 mg/kg (range 10–20 mg/kg)</td>
<td>maximum dose 600 mg/day</td>
</tr>
<tr>
<td>pyrazinamide (Z)</td>
<td>35 mg/kg (range 30–40 mg/kg)</td>
<td></td>
</tr>
<tr>
<td>ethambutol (E)</td>
<td>20 mg/kg (range 15–25 mg/kg)</td>
<td></td>
</tr>
</tbody>
</table>

Rationale: “Young age influences drug metabolism: a particular dose of a drug in mg/kg when given to a young child (under 5 years) may not reach the same level in the blood as when given to an older child or adult. Higher mg/kg dosages are therefore required in young children to achieve levels that are considered to produce effective bactericidal activity...revised dosages have an excellent safety profile and are not associated with an increased risk of toxicity”
Problem: The Childhood TB Treatment Market is “Broken”

- Forecasting challenges, low volumes, and inconsistent orders
- Manufacturers delay production until reach critical volume
- Low volume of sales potentially drives price up
- High prices and delays reduce demand
- Regulatory challenges lead to delays and hurdles
- Procurement fragmented between different suppliers and different treatment approaches

LOW DEMAND: COMPANIES LOSE INTEREST/EXIT THE MARKET
But No Manufacturers Entered This Market...Why?

• “There’s limited demand for pediatric TB formulations”:  
  – Orders are small  
  – Orders are irregular  
  – Wastage

• Lack consensus/switching guidelines

• Access challenges:
  – Registration processes are challenging:  
    • Long, many hurdles, inconsistent requirements in different countries
But country feedback suggests there IS a need for these products...

• “Why is it so difficult to get pediatric formulations” (Pediatric Association, Pakistan)

• “Crushed adult pills and extemporaneous preparation are used for treatment”; there’s a priority need for “child-friendly formulations” (NTP, Thailand)

• “China has no standard dosage of anti-TB drugs for children, medication is unreasonable.” There is a need for “availability and sustainability of child-friendly drugs” (NTP, China)

• Priority is the “use of FDCs for children” (NTP, Philippines)
How can we break the vicious cycle and create a virtuous cycle to ensure sustainable access to child-friendly TB formulations?

And other priority TB medicines?...

Countries harmonize guidelines; place regular orders in significant volumes.

Manufacturers maintain steady production.

Low costs and steady supply maintain or increase demand.

High volume creates “economy of scale” keeping cost low.

Countries have good quantification & forecasting.
Speeding Treatments to End Pediatric TB (STEP)-TB

Catalyzing availability of and access to child-friendly TB formulations

Unmet Medical Need

Not enough kids being treated – and not being treated appropriately

Goal

Increase access to correctly dosed, properly formulated, affordable, high quality pediatric TB medicines

Implementing Partner

World Health Organization

Timeline

High quality, child-friendly, properly dosed HRZ, HR and E products available by early 2016
Progress in Advancing Access to Appropriate Treatments for Childhood TB

2013: Project Launch

Q1 2014: Initiate discussions with GDF, Global Fund, other donors

Q2 2014: Three manufacturing partners secured

Q1 2015: Manufacturers submit for WHO PQ and begin local registration

Q2 or 3 2015: First-line FDC products available to procure through GDF

Q4 2014-2015: Disseminate WHO dosing guidelines in regional meetings

Q1-4 2015: Technical/planning support for countries

Q2 2016: First-line products WHO pre-qualified and available in the market
New Correctly-Dosed Pediatric Formulations

- Rifampicin 75 mg + Isoniazid 50 mg + Pyrazinamide 150 mg
- Rifampicin 75 mg + Isoniazid 50 mg

- Availability: mid to late 2015 through Expert Review Panel (ERP) and through Global Drug Facility (at least one manufacturer)
- Registration: submit for WHO Prequalification by early 2015 (at least two manufacturers); pursue local registrations in parallel
- Formulation: fixed dosed combination; dispersible; flavors—mango, strawberry, raspberry
- Price: close to currently available pediatric products, dependent on anticipated volumes
How Can Countries Help Ensure Availability of and Access to New Formulations?

- Adopt and scale up WHO dosing guidelines for childhood TB
- Raise awareness about the benefits of new formulations with regulators to facilitate registration
- Proactive quantification of needs
- Proactive budgeting and/or grant requests for procurement and scale up
- Timely order of formulations upon availability
- Request technical support as needed