Setting the Scene on Introduction and Scale-Up of TB Medicines for Children

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High-Level Dialogue on Pediatric HIV and TB in Children Living with HIV
6 November, 2020
Session Outline

• Importance of TB Stakeholder Alignment and Coordination
• TB Medicine Supply Situation
• Introduction of New TB Medicines and Regimens
• Reminder: Treatment Targets versus Treatment Reality
• Lessons Learned and What’s Needed Now
Stakeholder Alignment & Coordination Via TPMAT

TB Procurement and Market-Shaping Action Team (TPMAT)

Comprised of: procurers, donors, implementers, international organizations, NGOs, WHO, civil society, NTPs

End-To-End Life-Cycle Management
GDF-WHO-GF TB MEDICINES DASHBOARD: Paediatric DR-TB Formulations

Key Reference Tool

- Organizes, stores, displays info from >15 different sources
- Provides Roadmap for Prioritization, Harmonization, and Improving Access
- Guides NTPs with Selection, Rational Use, Benchmarking

http://www.stoptb.org/gdf/medicinesdashboard/
Key TB Medicine Harmonization/Prioritization Results Since 2018

Changes in “Guidance” Docs:

WHO Model EML and EMLc
- Complete TB overview
- 35 changes

WHO PQ EOI
- 20 changes

GF ERP EOIs
- 43 changes over past 5 rounds

GDF Catalog
- 27 changes
  - 13 additions, 14 deletions

5 TB Medicines Prioritized Through GF ERP Ad-Hoc Review Process and Available for Procurement

- 2nd supplier paediatric FDC for DS-T, LTBI – increased competition, supply security
- First clofazimine tablets (50mg and 100mg) – increased supply security, more suitable for children
- Second supplier clofazimine 100mg capsule – increased supply security
- 3HP FDC for TPT – new product, improved adherence
Supply: QA Child-Friendly Formulations for DS-TB and TB Preventive Treatment

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Dispersible</th>
<th># QA Suppliers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethambutol 100mg</td>
<td>Yes</td>
<td>1*</td>
</tr>
<tr>
<td>Ethambutol 100mg</td>
<td>No</td>
<td>3</td>
</tr>
<tr>
<td>Isoniazid 100mg</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>Isoniazid 100mg</td>
<td>No</td>
<td>7</td>
</tr>
<tr>
<td>Rifampicin 150mg</td>
<td>No</td>
<td>6</td>
</tr>
<tr>
<td>Rifampicin/Isoniazid, 75mg/50 mg</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>Rifampicin/Isoniazid/Pyrazinamide, 75mg/50mg/150mg</td>
<td>Yes</td>
<td>1</td>
</tr>
</tbody>
</table>

*Second formulation in WHO PQ Pipeline
Supply: 13 Child-Friendly DR-TB Formulations, Despite Tiny Market Size

<table>
<thead>
<tr>
<th>WHO Classification</th>
<th>Medicine</th>
<th>Formulation</th>
<th>Dispersible</th>
<th># QA Suppliers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>Levofloxacin or Moxifloxacin</td>
<td>Levofloxacin 100mg Moxifloxacin 100mg</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Bedaquiline</td>
<td>Bedaquiline 20mg</td>
<td>Yes**</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Linezolid</td>
<td>Linezolid 150mg Under development</td>
<td>Yes</td>
<td>0</td>
</tr>
<tr>
<td>Group B</td>
<td>Clofazimine</td>
<td>Clofazimine 50mg</td>
<td>Yes**</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Cycloserine or Terizidone</td>
<td>Cycloserine 125mg</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Group C</td>
<td>Ethambutol</td>
<td>Ethambutol 100mg</td>
<td>Yes</td>
<td>1*</td>
</tr>
<tr>
<td></td>
<td>Delamanid</td>
<td>Delamanid 50mg Delamanid 25mg Expected in 2021</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Pyrazinamide</td>
<td>Pyrazinamide 150mg</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Ethionamide or Prothionamide</td>
<td>Ethionamide 125mg</td>
<td>Yes</td>
<td>2</td>
</tr>
</tbody>
</table>

*Second formulation in WHO PQ Pipeline

**Product label is not dispersible
Stop TB/GDF Paediatric Drug-Resistant Tuberculosis Initiative

3-Pronged Approach to Expedite Product Introduction:

1. Identify early adopters and build demand
   • GDF provided a small contract to Sentinel Project on Paediatric Drug-Resistant TB for clinical support
   • In-kind programmatic support from KNCV, MSF
   • GDF doing quantification, forecasting, phase-in plans, ongoing procurement & supply plans

2. Match supply with demand
   • GDF working with suppliers to decrease batch sizes, lower prices; production planning
   • GDF pooling orders to meet minimum order quantities

3. Procurement support for initial purchases via GDF grants
Paediatric DR-TB and the Role of Pooled Procurement

On the Supply Side:
- Need 5 medicines to treat DR-TB
- Batch sizes vary for each medicine
  - 10-fold variation: 70-700 treatment courses
- Suppliers want to sell a full batch; otherwise,
  - Price and/or lead time will increase of
    remaining shelf life will be low

On the Demand Side:
- >60% countries treat < 20 kids per year
- A high-volume country treats ~100 kids
- No single country has sufficient demand to
  achieve optimal price and supply terms

GDF Pooled Procurement:
- Aligns supply (batch sizes) with global demand
  - Derisks suppliers
  - Ensures reliable, optimal, timely products
    and prices for NTPs
62 Countries Procuring Child-Friendly DR-TB Formulations via GDF’s Paediatric DR-TB Initiative

3. Armenia 23. Haiti 43. Pakistan
4. Azerbaijan 24. India 44. Papua New Guinea
5. Bangladesh 25. Indonesia 45. Paraguay
9. Cameroon 29. Lesotho
10. Chad 30. Liberia
11. Côte d’Ivoire 31. Madagascar
12. DRC 32. Malawi
13. Djibouti 33. Maldives
14. Dominican Rep. 34. Mali
15. Eq. Guinea 35. Mongolia
17. Eswatini 37. Mozambique
18. Ethiopia 38. Myanmar
20. Georgia 40. Nepal
27. Kenya
28. Kyrgyzstan
29. Lesotho
30. Liberia
31. Madagascar
32. Malawi
33. Maldives
34. Mali
35. Mongolia
36. Morocco
37. Mozambique
38. Myanmar
39. Namibia
40. Nepal
41. Niger
42. Nigeria
43. Pakistan
44. Papua New Guinea
45. Paraguay
46. Philippines

New country in 2020

Funding: Government of Japan and USAID
GDF Implementing Partners: Sentinel Project, KNCV, and MSF
Uptake Comparison of New Pediatric TB Formulations

# Countries Placing 1st Order (cumulative)

# Countries Ordered in First 15 Months:
- 1st Pedi FDC for DS-TB: 36
- 2nd Pedi FDC for DS-TB: 40
- New Pedi Meds for DR-TB: 56
## Paediatric TB – Treatment Targets vs Treatment Reality

<table>
<thead>
<tr>
<th>2022 Targets</th>
<th>2019 Treatment Estimates</th>
<th>2019 Disease Burden Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat 3.5 million children with TB</td>
<td>500,000 children treated</td>
<td>1.2 million new pedi TB cases</td>
</tr>
<tr>
<td>Treat 115,000 children with DR-TB, Including ~47,000 children &lt; 5 yo</td>
<td>~9,000 children treated for DR-TB, Including ~500* children &lt;5 yo</td>
<td>30,000 new pedi DR-TB cases, Including ~12,000* in &lt;5 yo</td>
</tr>
<tr>
<td>Provide preventive treatment for TB to 4 million children &lt; 5 yo by 2022</td>
<td>~433,000 children &lt;5 yo treated</td>
<td></td>
</tr>
</tbody>
</table>

*Estimate; data for children <5 yo not provided in Global TB Report

Biggest gap of missing people with TB is in kids under 5 yo, where 65% of kids are missing
Lessons Learned

• A tiny market size doesn’t need to be a barrier to development of child-friendly formulations

• But pooled procurement a MUST for such low-volume medicines

• Market stewardship with end-to-end visibility and organization harmonization are critical - especially when phasing-out old formulation(s) and phasing-in a new formulation(s)

• Very few missing formulations, but
  • Taste-masking inconsistent or absent across formulations; acceptability is unknown
  • New research findings may result in need for new formulations, pending WHO review
  • Strategic market planning and coordination will be needed to choose optimal formulations and engage suppliers to maintain and not reverse current market evolution

• TB Community – especially paediatric community– already well coordinated and well positioned to expedite and expand access to TB treatment
What’s Needed Now

• Broad-based commitment to prioritize children – address stigma & discrimination; build treatment literacy, advocacy, awareness
• Set and meet realistic but ambitious targets
• **Investments to increase case-finding and enrollment of children**
  • Better diagnostics
  • Household post-exposure management of children to identify kids who need treatment and prevention using family-friendly models
  • Donor recognition that innovation isn’t just about developing new tools
• Improved reporting and recording to support finding missing kids; disaggregation of disease burden and treatment data for kids < 5 yo; data on TB/HIV coinfection
• Research to fill treatment and dosing data gaps in children
• Acceptability research to guide paedi TB target product profiles, ensure product consistency in development
• Derisk and incentivize suppliers in a manner that doesn’t distort the market; ensures fair competition
• Dedicated funding to catalyze and expedite uptake of new formulations
• New approach for registration (or waivers) for such low-volume products
Thank you

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