New TB drugs and the private market

William Wells, Ph.D.
Director, Market Access, Global Alliance for TB Drug Development

7th Subgroup Meeting on PPM, Lille, France
October 23rd, 2011
The size and complexity of private sector TB drug sales
The private sector is a black box for TB treatment

- TB must be treated with an uninterrupted, multi-drug regimen. Therefore, should treatment be a public sector responsibility? But the private sector continues to draw clients.

- Private sector problems with quality: 100 private providers prescribed 80 different regimens; inappropriate regimens 89% of the time; financial considerations often prevent treatment completion.

- Public-private mix (PPM) brings public sector treatment norms to the private sector, through referrals or free drugs, but its reach is limited.

The Global Alliance for TB Drug Development (TB Alliance) is supporting development of new TB regimens. The private sector will pick up on new TB treatments, but we had no overview of current private sector behaviour in TB.
The overall goal of this study* was to understand TB drug sales in the private sector in 10 high burden countries.

**KEY PROJECT OBJECTIVES**

- **Define “private sector”:** channels outside of NTP influence (patients may pay cash or be insured/reimbursed)
- **Define data collection channels:** outlets covered by IMS data, including hospitals, pharmacies, drug stores etc
- **Define overlap:** Private sector channels that are monitored by IMS constitute the study universe

**Research Approach**

- **Volume and Sales (1st and 2nd line)**
- **FDC usage**
- **Strength variation**
- **Key manufacturers**

**Research Areas**

- **Cost per treatment course**
- **Formulation variation**
- **Fluoroquinolone market share**

*Wells et al., PLoS ONE 6:e18964 (2011)*
We included all high burden countries with IMS data available, except for Brazil.

<table>
<thead>
<tr>
<th>Rank of Overall TB Burden*</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>India</td>
</tr>
<tr>
<td>2</td>
<td>China</td>
</tr>
<tr>
<td>3</td>
<td>Indonesia</td>
</tr>
<tr>
<td>5</td>
<td>South Africa</td>
</tr>
<tr>
<td>6</td>
<td>Bangladesh</td>
</tr>
<tr>
<td>8</td>
<td>Pakistan</td>
</tr>
<tr>
<td>9</td>
<td>Philippines</td>
</tr>
<tr>
<td>11</td>
<td>Russian Federation</td>
</tr>
<tr>
<td>12</td>
<td>Vietnam</td>
</tr>
<tr>
<td>18</td>
<td>Thailand</td>
</tr>
</tbody>
</table>

*Overall burden includes both public and private sector in each country.
India is the most important private market

- 63% of the 10-country market is India alone; 85% is India, China and Indonesia.
1st line private markets are variable and, in some countries, LARGE [Measured relative to each country’s TB burden]

- These 10 countries = 60% of global burden.
- Average 67% public sector case detection.
- Average 66% of incidence potentially covered by private sector drugs.
1st line private markets are variable and, in some countries, LARGE [Measured relative to each country’s TB burden]
FDC strengths and combinations vary widely, especially in India, the Philippines and Pakistan

<table>
<thead>
<tr>
<th>Country</th>
<th>RH</th>
<th>HE</th>
<th>HZ</th>
<th>RHE</th>
<th>RHZ</th>
<th>RHZE</th>
<th>Total in Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>15</td>
<td>2</td>
<td>8</td>
<td>15</td>
<td>8</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Pakistan</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td></td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Bangladesh</td>
<td>5</td>
<td></td>
<td>4</td>
<td>1</td>
<td></td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Vietnam</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>4</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>2</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Russia</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>10-country Total</strong></td>
<td>20</td>
<td>13</td>
<td>1</td>
<td>11</td>
<td>18</td>
<td>11</td>
<td>74</td>
</tr>
</tbody>
</table>

Non-standard strengths represent >30% of total private sector TB drug volume.
Private market commercialization options for new TB drugs
Importance of addressing private sector uptake of new TB drugs

• Private sector TB treatment is dangerously variable and, in some countries, a major factor.

• Private sector often seeks out innovation first, and has a recognized problem with retention so short regimen appealing.

• Private sector sales of a new TB drug could maximize access but reduce the effective lifetime of the drug.
How can the health sector prepare for the introduction of new TB drugs?

- How to mitigate this threat to new TB drugs? First category of response is to improve the current delivery landscape
  - Expansion of public-private mix (PPM) programs
  - Expand the reach of public TB programs
  - Improve regulatory oversight for marketing approvals
  - Expand public sector diagnosis and treatment of MDR-TB
  - Improve the quality of care in the private sector, e.g., less fragmentation (franchises etc), better financing (insurance, vouchers, contracting), and integrate high quality TB treatment into these mechanisms.
New TB drug commercialization strategies in the private sector (1)

- Second strategy is to design appropriate commercialization models for new TB drugs.
- Moxifloxacin is already used for other indications, and will be off patent, so very limited control.
- Appropriate use can be encouraged via use of FDCs (difficult with REMoxTB regimens) and appropriate packaging.
- More expensive drugs, if properly subsidized, could provide a greater incentive to enroll in PPM.
- What activities can we undertake to improve the private sector situation for roll-out of off-patent drugs?
New TB drug commercialization strategies in the private sector (2)

- For **new, patent-protected** drugs that are registered initially for TB, more control is possible.
- Should pharma be encouraged to market these drugs to the private sector? In which countries?
- Should the private sector be allowed unrestricted access? Restricted access?
- Under what conditions?
- Are there practical means to administer these conditions?
- If PPM programs are limited, what should be the approach? Who should be the driver?
- Is PPM the only way to ensure quality delivery?
A combined strategy for drugs and diagnostics

- If drug sensitivity is determined prior to treatment, cure can be maximized and resistance generation can be minimized.
- DST and treatment capacity should grow together, and in coordination with each other.
- New diagnostics and drugs could be introduced to the private sector as a package, contingent on reporting outcomes to the public sector.
Summary

Recognizing that TB drug private markets are large and have variable practices, we need strategies for introducing:

- New, off-patent TB drugs.
- New, patent-protected TB drugs
- New TB diagnostics and drugs together.
Back-up slides
On average, around 35% of the 1\textsuperscript{st} line volume in the private sector does not have strengths identical to or multiples of GDF/NTP strengths.

- 111 total dosages (70 in India alone) vs 14 needed.
Countries use different strength forms for loose drugs

<table>
<thead>
<tr>
<th>Country</th>
<th>R</th>
<th>H</th>
<th>Z</th>
<th>E</th>
<th>Total in Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Philippines</td>
<td>6</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>Indonesia</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>China</td>
<td>8</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Pakistan</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Thailand</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Russia</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>South Africa</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Vietnam</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

10-country Total | 11 | 9 | 8 | 9 | 37

With daily or intermittent dosing, weight bands, an old and incomplete evidence base, and variable practices between countries, it becomes challenging to distinguish rational from non-rational use.
Three manufacturers produce certain FDC products that are pre-qualified by WHO but not all of this volume is prequalified.

Certain FDC products from 3 MNFs are prequalified by WHO:

- LUPIN
- MACLEODS PHARMA
- SANDOZ

- By MNFs that are not pre-qualified by WHO
- “Best-case” Scenario – Ceiling %
- Not all strengths by the same MNF are prequalified
- Not all facilities by the same MNF are prequalified
- Not all production lines in these facilities are high quality

Actual % of WHO-prequalified products <4%
Fluoroquinolones, but not MDR-TB regimens, cover a significant number of TB patients in India, Pakistan and Indonesia.

- Most of this FQ use is likely to be without other second line drugs.
- One third or more is ciprofloxacin, which is not recommended.
Conclusions

• Private markets are:
  • Large, at least in some countries, with volumes equal to or exceeding public sector volumes;
  • Dominated by a large number of local manufacturers of unknown quality, though FDC market more international and more concentrated;
  • Filled with a confusing mix of drug strengths (111 first line dosages and combinations) that are likely to further increase incorrect prescribing; and
  • Not covering the current gap in MDR-TB treatment. Prescribers may be adding single drugs to failing regimens, leading to further resistance.

• Possible interventions:
  • Restrict marketing authorization to logical and simple strengths;
  • Increase incentives, regulations, and enforcement to support quality manufacturing;
  • Boost the appeal of public programs;
  • Increase the scope of public-private mix (PPM) programs; and
  • Prioritize expansion of public MDR-TB treatment.