Target generic prices for novel treatments for drug-resistant tuberculosis

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New drugs are being developed for shorter course tuberculosis treatment, and for multi-drug resistant TB (MDR-TB).

Currently, treatment for MDR-TB can cost over $1000 US per patient-course in low income countries; far higher prices elsewhere.

Prices of treatments for MDR-TB and XDR-TB are straining health budgets.

However some of these drugs are close to patent expiry.

This study calculated target generic prices for novel TB treatments.
Patent Expiry Dates of key TB drugs

Group 1-3 drugs – already generic
Group 4 drugs – basic use patents expiring from 2014
Group 5 drugs – patent expiry 2016-2023

- **Moxifloxacin**: 2014
- **Linezolid**: 2014
- **Sutezolid**: 2014
- **Delamanid**: 2023
- **Bedaquiline**: 2023
- **Clofazimine**: Patent expired (but only one manufacturer)
  - **Linezolid**: 2014
  - **Sutezolid**: 2014
  - **Bedaquiline**: 2023
Methods

Online database: [www.infodriveindia.com](http://www.infodriveindia.com) shows costs per kg of exported API (active pharmaceutical ingredient). API costs obtained for all Group 1-4 drugs, linezolid and clofazimine.

We also collected prices by country, and from the Global Drug Facility (GDF)

**Sutezolid** – structurally similar to linezolid (single atom difference) similar costs of production assumed. **Posizolid** – structurally similar to linezolid, but 3X higher costs of production

**Delamanid and Bedaquiline** – analysis of routes of chemical synthesis, cost of raw materials and predicted yield

- **Pretomanid** – production cost assumed to be 4X higher than delamanid, based on chemical structure.
Methods – calculation of treatment cost

- Cost of API/kg
  - Grams of drug per month
    - Cost of API per month
      - Cost of excipients
        - Formulation packaging
          - Profit margin
            - Target price per month
Methods – low and high target prices

Lower target price
1c per pill for formulation
10c per month for packaging
10% profit margin

Volume demand assumption:
>1 million treatment courses / year
Validated from GDF price comparisons

Higher target price
4c per pill for formulation
35c per month for packaging
50% profit margin

Volume demand assumption:
>100,000 treatment courses / year
Validated from HCV cost analysis
## Group 1 and 2 drugs – current production costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patent</th>
<th>Daily dose</th>
<th>Exports 2014</th>
<th>API cost/kg</th>
<th>Target price</th>
<th>Current GDF price</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Expired</td>
<td>300mg</td>
<td>86,000 kg</td>
<td>$13-$38/kg</td>
<td>$0.8-$3.1</td>
<td>$0.6/month</td>
</tr>
<tr>
<td>Pyrizinamide</td>
<td>Expired</td>
<td>1600mg</td>
<td>137,000 kg</td>
<td>$20-$28/kg</td>
<td>$3.9-$11</td>
<td>$2.3/month</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Expired</td>
<td>1200mg</td>
<td>305,000 kg</td>
<td>$40-$49/kg</td>
<td>$5.1-$11.5</td>
<td>$2.8/month</td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Expired</td>
<td>1000mg</td>
<td>6.9m vials</td>
<td>n/a</td>
<td>$7.3-$47.2</td>
<td>$38.6/month</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>Expired</td>
<td>1000mg</td>
<td>2m vials</td>
<td>n/a</td>
<td>$13.2-$52.8</td>
<td>$25.2/month</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>Expired</td>
<td>1000mg</td>
<td>0.9m vials</td>
<td>n/a</td>
<td>$108-$173</td>
<td>$138/month</td>
</tr>
</tbody>
</table>
## Group 3 and 4 drugs – current production costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>patent</th>
<th>Daily dose</th>
<th>Exports 2014</th>
<th>API cost/kg</th>
<th>Target price</th>
<th>Current GDF price</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Expired</td>
<td>1000mg</td>
<td>91,000 kg</td>
<td>$110-$268/kg</td>
<td>$7.4-$19.7</td>
<td>$3.9/month</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>2014</td>
<td>400mg</td>
<td>37,000 kg</td>
<td>$180-$360/kg</td>
<td>$3.5-$9.4</td>
<td>$18.1/month</td>
</tr>
<tr>
<td><strong>Group 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothionamide</td>
<td>Expired</td>
<td>750mg</td>
<td>600kg</td>
<td>$118</td>
<td>$4.7-$10.5</td>
<td>$10.9/month</td>
</tr>
<tr>
<td>Cycloserine</td>
<td>Expired</td>
<td>750mg</td>
<td>900kg</td>
<td>$835-$1030</td>
<td>$21.3-$39.3</td>
<td>$27.7/month</td>
</tr>
</tbody>
</table>
Price of Moxifloxacin by country

- US (Bayer): $806
- US (generic): $232
- UK (Bayer): $106
- Spain (generic): $86
- Thailand (Bayer): $82
- South Africa (generic): $62
- France (generic): $38
- Russia (generic): $19
- GDF Catalogue (generic): $12
- India (nonSRA generic): $7
- Low-demand target price: $9
- High-demand target price: $3

Price in USD per month
## Group 5 drugs predicted production costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patent</th>
<th>Daily dose</th>
<th>Exports 2014</th>
<th>API cost/kg</th>
<th>Target price</th>
<th>Current GDF price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clofazimine</td>
<td>Expired</td>
<td>300mg</td>
<td>8,300 kg</td>
<td>$256/kg</td>
<td>$6.2-$16.4</td>
<td>$99/month</td>
</tr>
<tr>
<td>Linezolid</td>
<td>2014</td>
<td>600mg</td>
<td>11,000 kg</td>
<td>$175-$350/kg</td>
<td>$4.9-$12.8</td>
<td>$193/month</td>
</tr>
<tr>
<td>Sutezolid</td>
<td>2014</td>
<td>1200mg</td>
<td>None</td>
<td>$175-$350/kg</td>
<td>$4.9-$12.8</td>
<td>No prices</td>
</tr>
<tr>
<td>Posizolid</td>
<td>2019</td>
<td>600mg</td>
<td>None</td>
<td>$525-$1050</td>
<td>$11.4-$13.4</td>
<td>No prices</td>
</tr>
<tr>
<td>Delaminid</td>
<td>2023</td>
<td>200mg</td>
<td>None</td>
<td>$250-$500</td>
<td>$3.5-$8.6</td>
<td>$3,108*/month</td>
</tr>
<tr>
<td>Pretomanid</td>
<td>2016</td>
<td>200mg</td>
<td>None</td>
<td>$1000-$2000</td>
<td>$8.2-$21.2</td>
<td>No prices</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>2023</td>
<td>400mg</td>
<td>None</td>
<td>$2600-$3250</td>
<td>$8.8-$16.4</td>
<td>$136/month</td>
</tr>
</tbody>
</table>

*Little info available on pricing of delamanid – price in Japan quoted
Price of Linezolid by country

- US (Pfizer): $4,298
- Spain (Pfizer): $2,011
- UK (Pfizer): $1,862
- South Africa (Pfizer): $1,246
- Russia (Pfizer): $711
- Russia (generic): $690
- GDF Catalogue (generic): $150
- India (SRA-generic): $70
- India (nonSRA-generic): $17
- High Target: $13
- Low Target: $5

Price in USD per month.
Price of Delamanid by country

![Price of Delamanid by country](chart)

- **UK (Otsuka)**: $4,510
- **Germany (Otsuka)**: $4,258
- **Japan (Otsuka)**: $3,108
- **High target**: $9
- **Low target**: $4

Price in USD per month.
Price of Bedaquiline by region

- **High Income Countries**: $4,532
- **Middle Income Countries**: $453
- **Low Income Countries**: $136
- **High target**: $16
- **Low target**: $9

Assumed monthly dose is 28.4 x 100mg pills – average number per 28 days in STREAM arm C.
Potential prices for treatment courses

USD per patient for full treatment course

- Bedaquiline
- Clofazimine
- Levofloxacin
- Moxifloxacin
- Prothionamide
- Kanamycin
- Ethambutol
- Pyrazinamide
- Isoniazid

Bangladesh regimen

STREAM arm C

STREAM arm D
Potential prices for treatment courses

USD per patient for full treatment course

Current lowest price | HI | LO | Cost-based target prices

Pretomanid
Moxifloxacin
Pyrazinamide
1. Volume demand assumes that drugs for MDR-TB can be ordered centrally at low prices. Currently there are multiple drugs with different buyers, which limits the potential for savings. Low prices will depend on simplified market, with fewer drugs purchased, or standardised treatment courses.

2. There could be secondary patents enforced on some TB drugs, even after the basic patents have expired.

3. Target production prices for delamanid, pretomanid and bedaquiline were predicted based on routes of chemical synthesis and predicted yields – these estimates need to be validated by generic producers.

4. Upscaling production of some combination treatments could require pivotal clinical trial efficacy results: this may take another 2-4 years
Conclusions

1. There is the potential to produce combination treatments for MDR-TB for $100-$400 per patient-course.

2. There are currently large differences in TB drug prices between countries, even for drugs which should already be generic. Some drugs are available in India at prices well below GDF levels (e.g. moxifloxacin, linezolid).

3. Competitive large-scale generic manufacture could allow treatment of at least 10 times more MDR-TB cases while still operating within the procurement costs of current budgets. This would require overcoming patent barriers, competitive pricing and scaling-up surveillance and case detection to increase demand.