Implementation of MDR-TB Programme in India – Successes & challenges in 2nd Line Anti TB Drugs Management

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• Response of RNTCP to overcome challenges
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Introduction

• DOTS-Plus Programme initiated in India in 2007 in 2 states.
• DOTS-Plus guidelines for diagnosis & treatment of MDR-TB and drug logistics guidelines are in place.
• Treatment Regimen for MDR-TB :
  – Standardized Regimen.
  – 3 weight bands (16-25kg, 26-45 Kg and > 45 Kgs)
  – Intensive phase (6 to 9) months
    – Km (6 days/wk) / Levoflox/ Cyclo / Ethio / Etham / Z.
  – Continuation phase of 18 months
    \textit{Levo / Cyclo / Ethio / Etham}.
  – Daily Directly Observed Treatment.
<table>
<thead>
<tr>
<th>S. NO</th>
<th>Drugs</th>
<th>Phase</th>
<th>16-25 Kg</th>
<th>26-45 Kg</th>
<th>&gt;45 Kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Kanamycin-500/1000 mg</td>
<td>I.P</td>
<td>500 mg</td>
<td>500mg</td>
<td>750mg</td>
</tr>
<tr>
<td></td>
<td>(PC-17/PC-27)</td>
<td></td>
<td></td>
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<tr>
<td>2.</td>
<td>Levofloxacin-250/500mg</td>
<td>I.P &amp; C.P</td>
<td>200 mg</td>
<td>500mg</td>
<td>750 mg</td>
</tr>
<tr>
<td></td>
<td>(PC-28 / PC-29)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Ethionamide-250mg</td>
<td>I.P &amp; C.P</td>
<td>375mg</td>
<td>500mg</td>
<td>750 mg</td>
</tr>
<tr>
<td></td>
<td>(PC-20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Cycloserine-250 mg</td>
<td>I.P &amp; C.P</td>
<td>250 mg</td>
<td>500 mg</td>
<td>750Mg</td>
</tr>
<tr>
<td></td>
<td>(PC-24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Ethambutol-200/800 mg</td>
<td>I.P &amp; C.P</td>
<td>400 mg</td>
<td>800 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td></td>
<td>(PC-21 / PC-10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Pyrazinamide-500/750 mg</td>
<td>I.P</td>
<td>500 mg</td>
<td>1250 mg</td>
<td>1500 mg</td>
</tr>
<tr>
<td></td>
<td>(PC-8 / PC-23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Na PAS (PC-25 /PC-32)</td>
<td>I.P</td>
<td>5 g</td>
<td>10 g</td>
<td>12 g</td>
</tr>
<tr>
<td>8.</td>
<td>Pyridoxine-50/100 mg</td>
<td>I.P &amp; C.P</td>
<td>50 mg</td>
<td>100 mg</td>
<td>100mg</td>
</tr>
<tr>
<td></td>
<td>(PC-31 /PC- 26)</td>
<td></td>
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</table>
Successes and Challenges

**Successes** –
- Currently, twelve states implementing DOTS-Plus Programme in India.
- 3593 patients initiated on treatment upto Dec 2010.

**Challenges:**
- Fewer patients initiated on MDR TB treatment than expected during early phase of Programme – risking excess of 2\textsuperscript{nd} line drugs,
- Accurate forecasting of 2\textsuperscript{nd} line drugs,
- Treatment for MDR-TB spread over 24 months,
- Delay in supplies of drugs,
- Ensuring Quality of drugs,
- Preventing stock-outs.
- 2\textsuperscript{nd} line drugs have shorter shelf life than 1\textsuperscript{st} line Drugs,
Response of RNTCP to overcome challenges

• **Challenge** - Fewer patients initiated on MDR TB treatment than expected during early phase of Programme – risking excess of 2\textsuperscript{nd} line drugs.

• **Response**
  - Streamlining MDR-TB suspect identification and referral,
  - Introduced rapid LPA MDR-TB diagnosis, reducing diagnostic delay and patient attrition,
  - Improved planning for future utilization through data-driven State-level micro-planning, incorporating all aspects of DOTS PLUS Programme (geographic and time-based expansion of services, MDR-TB suspect identification, laboratory capacity, drug availability etc.),
  – Plan estimating the number of MDR-TB patients to be placed on treatment till 2014 made by Programme.
Diagnosis & Treatment Initiation Status of MDR TB – Year 2007 to 2010

### Cumulative Status

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>MDR TB Suspects tested</td>
<td>19199</td>
</tr>
<tr>
<td>MDR TB Cases Detected</td>
<td>5324 (28%)</td>
</tr>
<tr>
<td>MDR TB Cases Initiated on Treatment</td>
<td>3593 (68%)</td>
</tr>
</tbody>
</table>
Plan for patients to be tested and treated for MDR-TB

% S+ retreatment patients for DST

Drugs ordered are available in next yr

*Based on RNTCP 2012 goal of MDR diagnosis for all S+ retreatment patients,
Resource mobilization

- Lab scale up to be undertaken with support from:
  - UNITAID Expand TB
  - Global Fund –RCC and Rd 9
  - World Bank
  - USAID through WHO

- Second line drugs

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<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Global Fund –RCC</td>
<td>800</td>
<td>1200</td>
<td>2450</td>
<td>3500</td>
<td>4250</td>
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<tr>
<td>World Bank</td>
<td>2350</td>
<td>3450</td>
<td>4550</td>
<td>9000</td>
<td>13250</td>
</tr>
<tr>
<td>UNITAID</td>
<td>4850</td>
<td>5000</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Global Fund Rd 9</td>
<td>-</td>
<td>5350</td>
<td>18000</td>
<td>17500</td>
<td>14500</td>
</tr>
<tr>
<td>Total</td>
<td>8000</td>
<td>15000</td>
<td>25000</td>
<td>30000</td>
<td>32000</td>
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</tbody>
</table>
• **Challenge - Accurate forecasting of 2nd line drugs**

• **Response –**

  – Drug Forecasting by Central TB Division alongwith Technical Assistance from partners of RNTCP.
  – Requirements worked out for all 3 weight bands,
  – Based on past experience, assumptions in weight gain & Prolongation of Intensive phase taken into account,
  – Regular validation as per latest data available from states,
  – Available stock balances taken into account while forecasting,
<table>
<thead>
<tr>
<th>Calculation Sheet for 2nd Line Drugs with 3 Weight Bands</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Expected Patients</strong></td>
</tr>
<tr>
<td><strong>Expected Patients in the 16-25 Kg weight band (5%)</strong></td>
</tr>
<tr>
<td><strong>Expected Patients in the 26-45 Kg weight band (65%)</strong></td>
</tr>
<tr>
<td><strong>Expected Patients more than 45 kg (30%)</strong></td>
</tr>
<tr>
<td><strong>Assumption In Weight Gain, i.e patients who move to higher weight band after 1 year of treatment</strong></td>
</tr>
<tr>
<td><strong>Assumption in IP Prolongation for 2 months</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>PC-17</th>
<th>PC-27</th>
<th>PC-28</th>
<th>PC-29</th>
<th>PC-24</th>
<th>PC-20</th>
<th>PC-30</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>16-25 Kgs</strong></td>
<td>1,020</td>
<td>3,120</td>
<td>720</td>
<td>3,120</td>
<td>3,120</td>
<td>3,120</td>
<td>3,120</td>
</tr>
<tr>
<td><strong>26-45 Kgs</strong></td>
<td>13,260</td>
<td>40,560</td>
<td>82,560</td>
<td>82,560</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>&gt; 45 Kg</strong></td>
<td>6,120</td>
<td>32,400</td>
<td>32,400</td>
<td>97,200</td>
<td>97,200</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>14,280</td>
<td>6,120</td>
<td>35,520</td>
<td>73,680</td>
<td>182,880</td>
<td>182,880</td>
<td>3,120</td>
</tr>
</tbody>
</table>
## Calculation Sheet for 2nd Line Drugs with 3 Weight Bands

<table>
<thead>
<tr>
<th></th>
<th>PC-32</th>
<th>PC-25</th>
<th>PC-21</th>
<th>PC-10</th>
<th>PC-8</th>
<th>PC-23</th>
<th>PC-31</th>
<th>PC-26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-25 Kgs</td>
<td>158</td>
<td>6,240</td>
<td>720</td>
<td>1,140</td>
<td>3,120</td>
<td>720</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26-45 Kgs</td>
<td>2,048</td>
<td>-</td>
<td>40,560</td>
<td>14,820</td>
<td>14,820</td>
<td>49,920</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 45 Kg</td>
<td>2,835</td>
<td>32,400</td>
<td>32,400</td>
<td>-</td>
<td>13,680</td>
<td></td>
<td>23,040</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2,835</td>
<td>2,205</td>
<td>38,640</td>
<td>73,680</td>
<td>15,960</td>
<td>28,500</td>
<td>3,120</td>
<td>73,680</td>
</tr>
</tbody>
</table>

### Expected Patients
- 100
- 16-25 Kg weight band (5%): 5
- 26-45 Kg weight band (65%): 65
- More than 45 Kg (30%): 30

### Assumptions
- Weight Gain: 40% patients
- IP Prolongation for 2 months: 80% patients
• **Challenge** – Treatment for MDR-TB spread over 24 months.
• **Response**
  - Community DOT providers identified and trained for ensuring adherence to treatment by patients.
  - Detailed guidelines for logistics management of 2\(^{nd}\) line Anti-TB drugs in place.
  - Training on DOT Provision and drug logistics management to field staff done regularly by Central TB Division and states.
Steps taken to improve drug logistics

- Detailed guidelines for logistics management of 2\textsuperscript{nd} line Anti-TB drugs finalised & being implemented.
- Loose drugs packaged into 3-monthly drug boxes for both IP & CP at State Drug Store only.
- Packaging of IP/CP boxes done under guidance of STO/Medical Officer/Drug logistics I/C at State level.
- One 3 monthly IP/CP box to have 3 divisions with 1 monthly box/pouch.
- Label on IP/CP boxes to clearly mention the following:-
  - Item-wise name of drugs with Quantity in the Box.
  - Batch No. & Date of Expiry (DOE) of individual drugs.
  - DOE of IP/CP box to be the expiry date of the drug containing shortest expiry.
  - Running Sl.No. & date of Issue on IP/CP box
Movement of 2nd line Drugs

State Drug Store--

- packing of loose drugs into IP/CP box

- Loose drugs supplied to DOTS-Plus site indoor facility monthly

- Stock of IP/CP PWB and PAS held at DTC

- PWB supplied to TU as per quarterly TU PMR

- Stock of IP/CP PWB and PAS held at TU with buffer

- PWB supplied to the DOT Centre under intimation to PHI by RNTCP staff

- IP/CP PWB and PAS received by the DOT Centre

- 3-monthly IP or CP Category IV PWB issued immediately to the respective DOTS-Plus provider

- Loose Drug supplied to the DOTS-Plus site to maintain adequate stock for a month of treatment, plus small buffer

- On Discharge, patient given a maximum of 7 Days Category IV drugs to cover transfer period

- Patient reports to the DTO. PWB supplied to DOTS Plus provider through MO-PHI

- Stock of IP/CP PWB & PAS supplied to DTC as per quarterly District PMR
Intensive Phase Box under DOTS-Plus
• **Challenge - Delay in 2nd Line Anti-TB Drug supplies**

• **Response**
  
  – **Procurement by RNTCP through two independent sources of drug supplies** (funded by Global Fund & World Bank respectively) ensure regular availability of drugs in the states:-

  1) For states funded by **Global Fund**, after approval from Green Light Committee (GLC), drugs procured through Global Drug Facility (GDF) by **IDA Foundation**

  For 2011, Application to GLC for enrolment of additional cohort of 11,550 MDR-TB patients submitted in March, 2011 and approved by GLC on 15th April, 2011 (total approved Cohort so far – 17,800).

  2) For **World Bank** funded states, drugs procured by **procurement agency of the Ministry of Health** (currently M/s RITES Ltd.)

  - Inter-state transfer of drugs to ensure optimum stock levels in all the implementing states at any given time.
• **Challenge** - Ensuring Quality of 2nd line Anti TB Drugs.

• **Response** –

Measures for ensuring Quality *(at the time of Procurement)*: -

- **For states funded by Global Fund,** procurement from drug suppliers *with WHO- Pre-Qualified Products* only.

- **For states funded by World Bank,** drugs procured through International Competitive Bidding (ICB), restricting procurement to WHO-GMP compliant suppliers only.
  - Verification of WHO-GMP Certificates by Joint inspection team under Drug Controller General of India.
  - Pre-dispatch inspection of all batches
Measures for ensuring Quality (Post-Procurement) : -

- Independent Laboratory for Quality Testing of 1\textsuperscript{st} & 2\textsuperscript{nd} Line Anti-TB Drugs hired by Programme (ISO 17025 certified).
- Zone-wise random samples drawn, as per defined protocol, every Quarter from
  - 1 GMSD (2 batches)
  - 1 State Drug Store
  - 4 District Drug Stores
- The contracted laboratory shall send the reports on the drug tests to the sender, with a copy to CTD, within 15 days of receipt of the drug samples.
- Reports presented to the Committee headed by National Drug Regulatory Authority (Drug Controller General - India).
- **Storage guidelines** shared with States for implementation – these include requirement of additional storage space, specifications for storage, stacking arrangements, control of humidity and temperature, waste disposal guidelines etc.
• **Challenge** - Preventing stock-outs.

• **Response**
  - Regular monitoring of drug stocks through monthly SDS Reports from implementing states & Quarterly Programme Management Reports from states & districts,
  - Regular Trainings to State and district level officials on Best Practices in Drug Logistics Management,
  - Supervisory visits and consultations with state & district officials.
MIS for 2nd Line Anti TB Drugs

Central TB Division

State Drug Store (SDS) / State TB Officer (STO)

District TB Center (DTC)

TB Unit (TU)

Monthly/Quarterly Reports

Quarterly Report

Monthly Report

DOTS Plus Site
• **Challenge** – 2\textsuperscript{nd} line Drugs have shorter shelf life than 1\textsuperscript{st} line Drugs.

• **Response**
  - Drugs received in 3 tranches (instead of usual 2) so as to ensure their full utilization within shelf-life.
  - Regular monitoring of 2\textsuperscript{nd} Line Drug stocks in various state drug stores by Central TB Division.
Results and lessons learnt

• Improved planning for number of MDR-TB patients to be diagnosed and placed on treatment in future,

• More than one source of 2nd line drug supplies ensures uninterrupted supply line,

• Drug logistics guidelines have evolved based on initial field experiences and regular consultations with state and district officials. These guidelines are dynamic & get revised based on new experiences from field,

• Regular reporting of stock status to higher level done by sub district (TU), district & state drug stores,

• As a result of all above, RNTCP has been able to prevent stock outs of these drugs in the concerned states.
Conclusions and key recommendations

To improve 2nd line Anti TB Drug logistics in a country, following is recommended:-

• Planning for no. of MDR-TB patients to be diagnosed and placed on treatment in future;
• Preferably have more than one source of drug supply;
• Drug logistics guidelines to be in place;
• Regular monitoring of drug stocks;
• Trainings to field staff;
• Supervisory visits and frequent consultations with state & district officials.
UNION CONFERENCE- BERLIN
Nov, 2010
THANK YOU