Patients and TB: Improving treatment outcomes through a patient centred approach and access to new treatments

5th TB Symposium – Eastern Europe and Central Asia
Ministry of Labour, Health and Social Affairs of Georgia
and Médecins Sans Frontières

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Access to DRTB drugs: current situation and challenges

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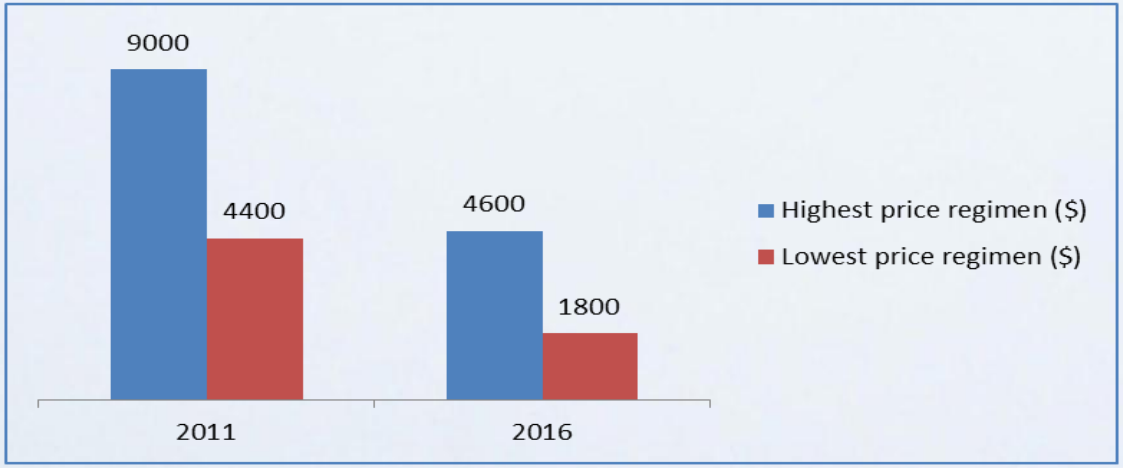
Agenda

- Current prices : improvements, but challenges persist
- New drugs and repurposed DR-TB drugs : remaining barriers blocking access
- Policy recommendations

Price improvement but challenges persist

- Decrease of preferred regimen prices since 2011



- But it could be priced as low as $100-$400 per treatment course based on a 'cost-plus' model [(1)]

[(1)] *Source: Gotham D et al. Target generic prices for novel treatments for drug-resistant tuberculosis. 15th Europeam AIDS Conference. Barcelona, abstract PS2/4, October 2015*

Price improvement but challenges persist

Improvement

- Capreomycin, linezolid, levofloxacin, Cycloserine price ↘
- due to ↗ of number of finished product manufacturers and/or API sources

Challenges

- Steady price since 2011: clofazimine, amikacin, prothionamide and ethionamide
- Increased price since 2011: Kanamycin, PAS sodium

New drugs

Two new drugs since 2012
but NO access yet for the majority of patients most in need.

- **Bedaquiline (Innovator: Janssen)**
  - Experience of use in Compassionate Use programmes (700 patients) (CU programme ended in Sept. 2015) and routine use (2300 patients)
  - Conditional approvals at EMA and USFDA
  - Included on the WHO EML
  - Treatment length : 6 months
  - Phase III Clinical trial has yet to commence (extended STREAM trial)
  - WHO recommendations [(2)] : Bedaquiline may be used as a Group 5 drug in addition to a regimen designed according to WHO recommendations

[(2)] *WHO - Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis*
http://www.who.int/tb/publications/pmdt_companionhandbook/en/

New drugs

- **Bedaquiline (Innovator: Janssen)**
  - First, a tiered pricing access strategy

    $900 LIC/3000 MIC/30,000 for 6 month course

    Then a donation programme launched April 2015 through USAID/GDF for 30.000 treatments for all Global Fund eligible countries
  - Registration process slow (registered in 9 and pending in 9 of 27 high burden countries).
  - IP barriers until 2029 limiting generic competition or development of FDCs

New drugs

- **Delamanid (Innovator: Otsuka)**
  - Global Compassionate Use programme but only 42 treated end of 2015. In total only about 180 patients have received delamanid outside of clinical trial
  - Conditional approval at EMA with broader recommendations for MDR patients (includes MDRTB with an increased risk of poor outcome)
  - Included on the WHO EML
  - Treatment length : 6 months
  - Delamanid's phase III clinical trial completed enrolment in November 2013, with results expected in 2017 unclear
  - WHO recommendations : Delamanid may be used as a Group 5 drug in addition to a regimen designed according to WHO recommendations

New drugs

- **Delamanid (Innovator: Otsuka)**
  - International donation programme (FighTBack) announced in April 2015 to give access to 20% of all diagnosed MDR-TB patients by 2020; details remain unclear
  - In February 2016, GDF and Otsuka announced a price of **$1700 per treatment** course, available to Global Fund eligible countries through the GDF (excluding Russia)
  - Registered in EU, Japan and South Korea but registration process still to commence in high burden TB countries
  - IP barriers until 2031 limiting generic competition or development of FDCs

Repurposed DRTB drugs

- **Linezolid (Innovator: Pfizer)**
  - Included on the WHO EML
  - Treatment length : 20 months
  - Pricing: $ 3253 per treatment course.

    Originator product prohibitively expensive.

    High price in high TB burden countries such as South Africa: price offered to SA is 17% to 46% higher than price offered to GDF
  - QA generic products slowly becoming more available
  - Not registered for TB
  - IP barrier (secondary patents) could preclude importation of low-cost generics until 2021 (but very likely will be ignored)

Repurposed DRTB drugs

- **Clofazimine (Innovator: Novartis)**
  - Not on the current WHO Essential Medicines List
  - Treatment length : 20 months
  - Pricing : $ 666 per treatment
  - Only one supplier of QA product, with restrictive access for TB
  - Not Registered for TB
  - In April 2014, USFDA agreed to review a filing under Orphan Drug designation by Novartis for phase II clinical trial, which could lead to registration of clofazimine with a TB indication by 2020

	WHO EML	Indication/ Registration	Lowest Gobal price Price	Competition	QA Supplier	Use
Linezolid (Pfizer)	YES	• No TB indication	$161, per patient, per month ($3253 per treatment)	YES	TWO QA (MORE TO COME)	Growing
Clofazimine (Novartis)	NO	• No TB indication	$66 (100mg) pppm ($666 per treatment)	NO	ONE QA	Growing
Bedaquiline (Janssen)	YES	• Conditional approval • DRTB • Registered 9, pending in 9, of 27 HBC	$150 pppm ($900 per treatment)	NO	ONE QA	Growing CU (700 patients) Routine use (2300 patients – Jan. 2016)
Delamanid (Otsuka)	YES	• Broader recommendation for MDR-TB • Conditional approval • Japan/EU/S Korea	283 pppm ($1700 per treatment)	NO	ONE QA	180 patients outside clinical trial

Policy recommendations

- **Affected countries**
- Scale up access to Group 5 medicines per WHO recommendations
- Register Group 5 medicines and new TB drugs, or at least in the short term allow import waiver to allow access (ex. Kyrgyzstan access to new drugs still pending)
- Update national TB Guidelines and Essential Medicines Lists (EML)
- Set up adequate regulations for Compassionate Use or expanded access programmes for new TB drugs
- **Global Fund**
- Allow countries to carry on procuring quality-assured TB medicines once they transition out from Global Fund support
- **Global Drug Facility**
- Push for alternative generic (Clofazimine) and promote generic competition (Linezolid)
- Promote best forecasting practices at country level
- Explore options allowing GDF bidding to national public TB medicine tenders

Policy recommendations

- **WHO**
- Pursue data collection (addition of clofazimine to the WHO EML)
- Promote fast track registration of WHO prequalified TB medicines as well as those registered by stringent regulatory authorities
- **Donors**
- Support countries upgrading national TB programmes guidelines and national EML to meet WHO recommendations
- Ensure DR-TB medicines procured are compliant with WHO quality standards
- **Pharmaceutical companies**
- Submit for registration of Group 5 and new TB drugs in all high burden TB countries
- Offer affordable, sustainable commercial prices and when applicable negotiate voluntary licences
- Avoid problematic donation programmes
- **Civil society**
- Ensure countries are procuring quality assured medications for DRTB programmes
- Pressure governments to upgrade national policies in line with WHO recommendations

DR-TB DRUGS UNDER THE MICROSCOPE

SOURCES AND PRICES FOR DRUG-RESISTANT TUBERCULOSIS MEDICINES

4th Edition – March 2016

ACCESS CAMPAIGN

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www.msfaccess.org

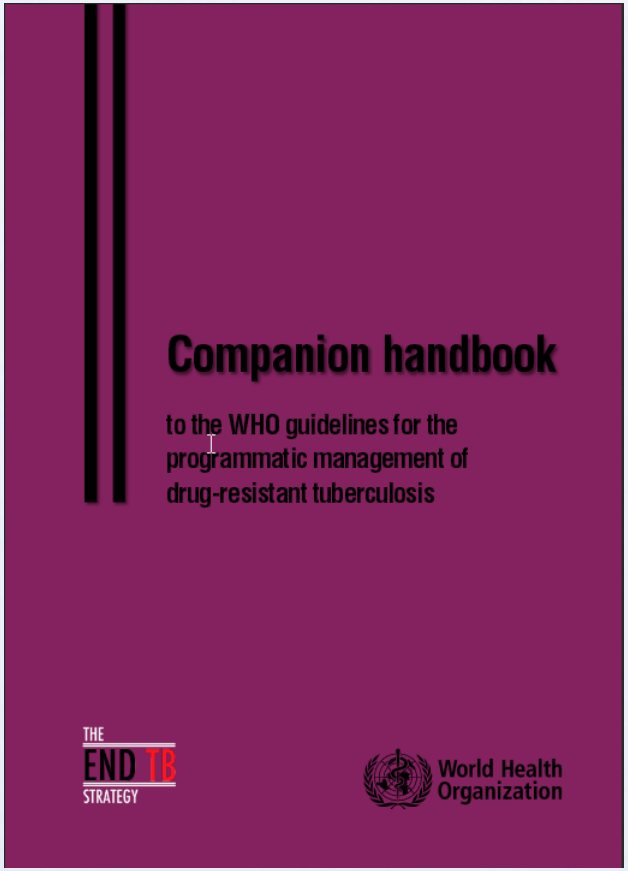
http://www.msfaccess.org/our-work/tuberculosis

Additionnal slide
New drugs indications WHO recommendations

Bedaquiline or delamanid may be used as a Group 5 drug in addition to a regimen designed according to WHO recommendations in patients presenting with:

- MDR-TB plus additional risk of poor outcomes (eg. Drug intolerability)
- MDR-TB plus resistance to fluoroquinolones
- MDR-TB plus resistance to both classes of Group 2 second-line injectable agents (aminoglycosides and polypeptides) or severe intolerance to second-line injectable agents
- MDR-TB plus two or more Group 4 (Eto, Pto, Cs, PAS) drugs compromized or severe intolerance shown to these drugs
- XDR-TB

➢ Refer to Annex 4.5 for a situation-based guide to choosing between bedaquiline and delamanid. Annexes 4.1 and 4.2 provide detailed descriptions for each drug in regimens that might be considered under various treatment scenarios.



http://www.who.int/tb/publications/pmdt_companionhandbook/en/