

Tuberculosis in 2017: Searching for new solutions in the face of new challenges

6th TB Symposium – Ministry of Health of the Republic of Belarus,
Republican Scientific and Practical Center for Pulmonology and Tuberculosis, and
Médecins Sans Frontières

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Access update, registration & procurement
strategies

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Access to bedaquiline

- Innovator: Janssen - Partnership in CIS countries: Pharmstandard
- No voluntary license yet with generic companies (Janssen's patent ends in 2029)
- **Jan. 2017: 7597 patients in programmatic use – 766 patients in compassionate use**
- Phase III Clinical trial (extended STREAM trial): results due by 2021

WHO interim guidelines (June 2013) based on current conditional approvals at EMA (March 2014) and USFDA (Dec. 2012)

Updated WHO guidelines expected Feb. 2017

Translation in national guidelines needed

Added on WHO EML for TB (May 2015)

Translation in national EML needed

Beyond USA & Western Europe, registration in 12 countries including Armenia, **Moldova**, Russian Federation, Turkmenistan & Uzbekistan

. On-going dossier assessment at Regulatory Authorities **in 17 countries, including** Belarus
 . Lack of Phase III, a problem in Azerbaijan, Kazakhstan, Kyrgyzstan; possibly Georgia?

- January 2015, for CIS countries: 6 month course at US\$ 1700 in the Russian Federation & US\$ 1351 in other CIS countries
- April 2015, for all GFATM eligible countries: USAID/Janssen donation through GDF for **30.000** treatments till spring 2019 (Jan. 2017: **6385** courses ordered)

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Access to delamanid

- Innovator: Otsuka - Partnership for CIS countries: under negotiation
- No voluntary license yet with generic companies (Otsuka's patent ends in 2031)
- **Jan. 2017: 469 patients in programmatic use – 1800 patients in compassionate use**
- Phase III Clinical trial: results due by Q4 2017

WHO interim guidelines (Oct.2014) based on current conditional approvals at EMA (April 2014); update for children (Oct. 2016)

Translation in national guidelines needed

Added on WHO EML for TB for adults (May 2015); submission for children (March 2017)

Translation in national EML needed

Beyond Japan & Western Europe, registration in **South Korea (Republic)**, Hong Kong

. On-going dossier assessment at Regulatory Authorities in China, Indonesia, Philippines, Turkey
 . Evaluation whether to go for EAEU harmonised procedure by Q2 2017

- February 2016, all GFATM eligible countries: 6 month course at US\$ 1700 through GDF (Jan. 2017: **1648** courses ordered)

Access to linezolid

- Innovator: Pfizer
- Secondary patents could preclude importation of low-cost generics until 2021, but very likely to be ignored
- Quality-assured generics: Teva, Hetero, Cipla (Macleods, still ERP status till Oct. 2017)
- No TB indication : repurposed medicine for DRTB

Upgraded as category C in the MDRTB
WHO guidelines (June 2016)

Translation in national guidelines needed

Added on WHO EML for TB (May 2015)

Translation in national EML needed

- May 2016: thanks to enhanced competition across manufacturers, **price drop (- 75%)** from US\$ 3253 per treatment course (20 months) to US\$ 838

Access to clofazimine

- Innovator: Novartis
- No patent barrier, nevertheless no quality-assured generics yet (2 companies developing generic versions, one could submit its dossier to WHO Prequalification Programme by Q2 2017)
- No TB indication yet (repurposed medicine for DRTB), though in Jan. 2017, USFDA granted fast-track assessment to Novartis's retrospective individual patient data due for submission by Q4 2017

Upgraded as category C in the MDRTB WHO guidelines (June 2016)	Translation in national guidelines needed
Submission to WHO EML for TB indication, adults & children (March 2017)	If successful, translation in national EML needed

- One set of price at Novartis, whatever the country: US\$ 666 per treatment (20 months)

Access to imipenem

- Innovator: MSD (USA)
- Quality-assured generics: at least Demo (Greece), Fresenius (UK), Labatec (Switzerland), Panpharma (France), Sun Pharma (India)
- No TB indication: repurposed medicine for DRTB

In category D3 (add-on agent) in the MDRTB WHO guidelines (June 2016)	Translation in national guidelines needed
On current WHO EML only as general anti-bacterial	-

- “Best” price so far through GDF at Panpharma: US\$ 3402 per treatment (for an average of 8 months)
- Major operational hurdle: need for infusion (Porth a Cath), with related complications for patient home care
- Transitory companion medicine to new DRTB ones till more efficient/safe new compounds are available?

Challenges in access

- **Green Lights easing up dispensation of new /repurposed DRTB medicines**
 - ✓ WHO guidelines on how to dispense new /repurposed DRTB medicines
 - ✓ Listing on WHO EML for TB (except clofazimine & *imipenem if DRTB need confirmed*)
 - ✓ Quality-assured (QA) sources on the international market
- **Red Lights blocking importation and/or dispensation of new /repurposed DRTB medicines**
 - ✓ Delay in updating national TB guidelines & EML
 - ✓ Lack of TB indication for repurposed medicines
 - ✓ Delay in national registration & lack of importation waiver provision
 - ✓ High cost per patient per month (best current prices for QA medicines)

When currently for moxifloxacin: US\$ 9 of cycloserine: US\$ 25,

Linezolid	Clofazimine	Bedaquiline (outside donation)	Delamanid	Imipenem
US\$ 42	US\$ 66	<u>Pharmstandard - CIS countries</u> US\$ 225 (CIS, not Russian Federation) US\$ 283 (Russian Federation only) <u>Janssen – non CIS countries</u> US\$ 150 (Low Income Countries) US\$ 500 (Middle Income Countries)	US\$ 283	US\$ 425

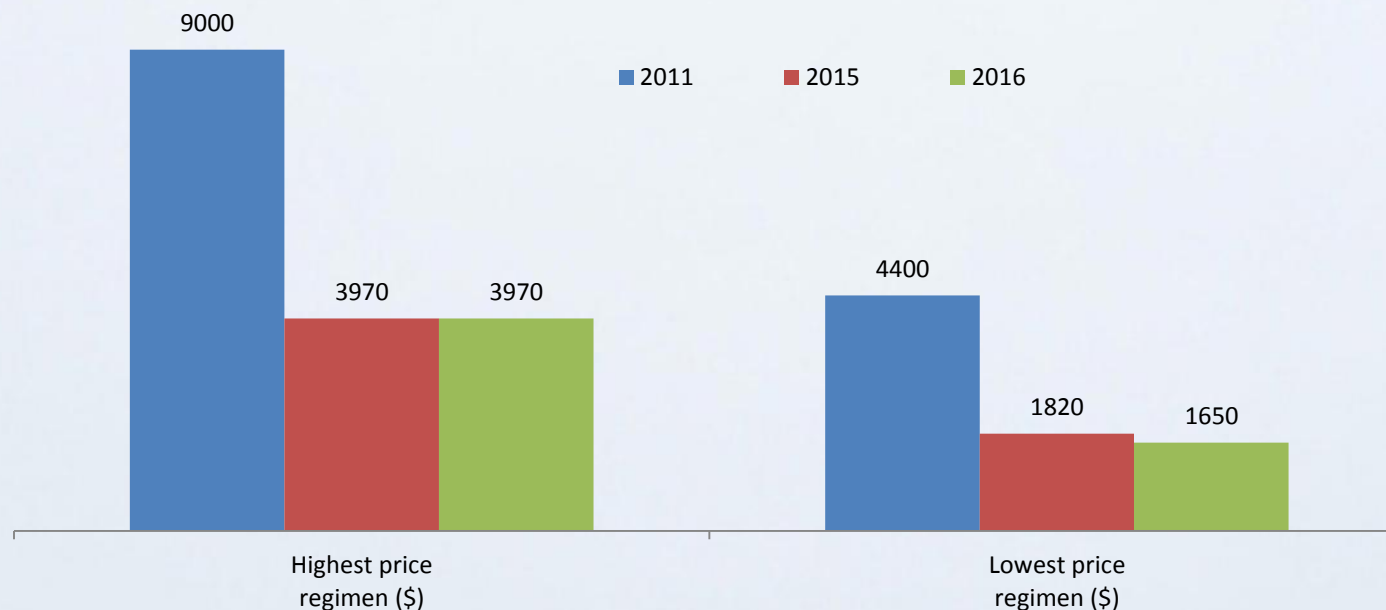
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How to do better on price?

- Considering the relatively small DRTB market, only one way forward:
competition across manufacturers & pooled procurement across countries
- **GDF, global example of pooled procurement of QAed TB medicines at the lowest global prices by setting up international yearly bids across manufacturers**

Decrease of preferred regimen prices through GDF from 2011 till 2016, in US\$:



Note: with 2016 GDF prices, short regimen cost: 600 to 800 US\$

- **Besides the Global Fund mechanism, how to keep GDF as a bidder in national public tenders?**

How to do better on regulatory components?

Early access mechanisms before local marketing authorisation is granted

✓ **Compassionate Use**

- . When no satisfactory authorised therapy in the context of a serious, life-threatening condition for patients who cannot enter a clinical trial
- . On an individual basis
- . Possible once Phase II data are available for a new medicine
- . Guidance in 2014 WHO Companion handbook to the WHO guidelines for the programmatic management of DRTB

✓ **Expanded Access**

- . Like Compassionate Use for a cohort of patients
- . Guidance in 2014 WHO Companion handbook to the WHO guidelines for the programmatic management of DRTB

✓ **Import waiver**

✓ **Temporary access under a national research framework**

How to do better on regulatory components?

Expedited registration (1/2)

✓ **Mutual recognition between regulatory authorities**

- Take benefit of assessment already performed by stringent regulatory authorities (SRA)

→ Example: bill N°4484 in Ukraine

« For public health priority diseases such as TB, the law allows medicines already authorized in the EU, United States, Japan, Australia, Canada and Switzerland to be authorized in Ukraine under a simplified procedure in less than a month »

✓ **Regional harmonisation framework**

- Eurasian Economic Union harmonised registration procedure for medicines

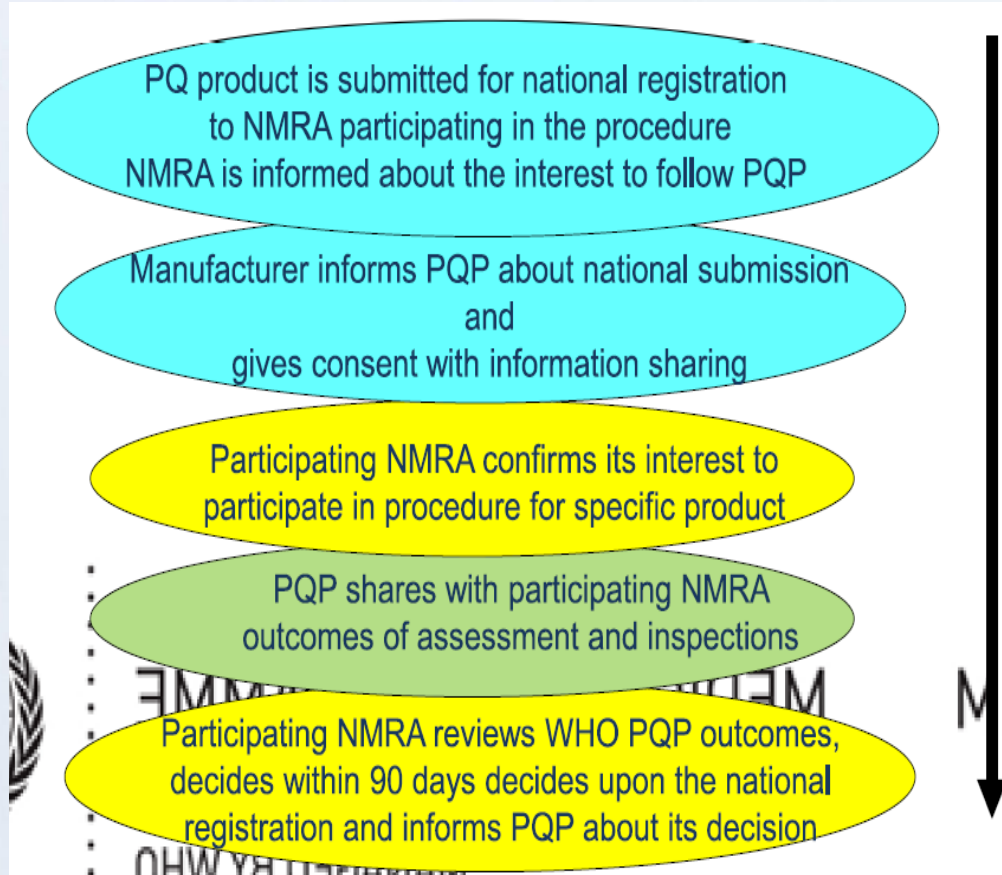
. To start by Q2 2017? (approval of chemical regulations still holding the process)

. So far Armenia, Belarus, Kazakhstan, Kyrgyzstan, Russian Federation are part of the process; will more CIS countries join?

How to do better on regulatory components?

Expedited registration (2/2)

✓ Collaborative Registration Programme with the support of WHO Prequalification



- For WHO prequalified & SRA registered medicines
- 30 participating countries, including Armenia, Georgia, Kyrgyzstan, Ukraine
- 185 marketing authorisation approved, including 46 for TB & DRTB medicines
- 93 days as a median time from information sharing to registration (2014 survey)