Policies and challenges related to the introduction of new drugs and regimens for DR−TB patients

August 6, 2015

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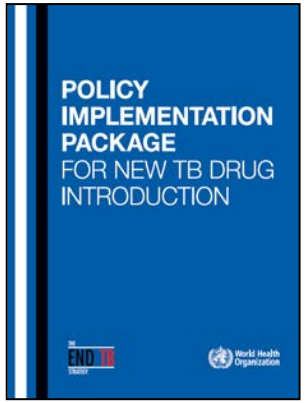
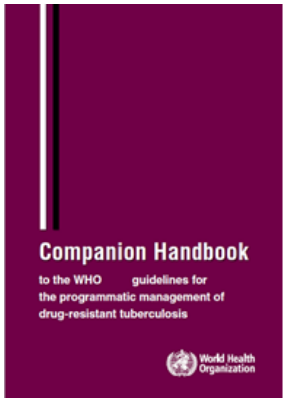
GLOBAL TB PROGRAMME

World Health Organization

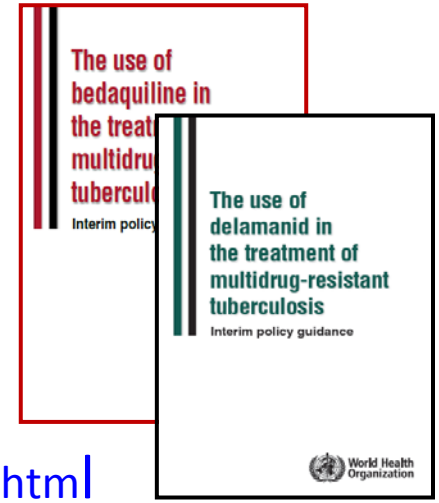
WHO's strategy and guidance for new TB drug introduction

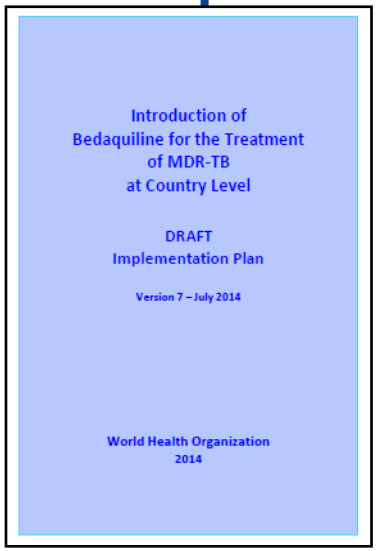




Strategic Plan for New TB Drug Introduction → **Standard Policy Development Framework** → **Expert Reviews** → **Interim guidance** → **Policy implementation Package** → **Support to Country Roll-out**

Bedaquiline (Jan 2013)
Delamanid (April 2014)





http://www.who.int/tb/new_drugs/en/index.html

The WHO Strategic Plan for rational introduction of new TB drugs and regimens in countries

Key Principles:

- Need for combination regimen(s)
- Adaptation to largely variable country settings (health & NTP infrastructure, TB epidemiology, level of preparedness, etc.)
- Ensure equitable access to safe and quality-assured new drugs for all patients in needs
- Prevent misuse of the drugs and emergence of resistance
- Multistage and pluri-partner process.

World Health Organization

Introduction and rational use of new drugs and drug regimens for TB treatment

CURRENT SITUATION

- Much progress has been made in research and development of new drugs for tuberculosis (TB) over the last decade.
- A series of Phase II and III trials of shortened treatment of drug-susceptible (DS) TB including re-purposed drugs (e.g. fluoroquinolones) or new dosages of known drugs (e.g. rifamycin, rifapentine) are presently on-going, with earliest results expected in 2013.
- Novel drugs are being evaluated in Phase IIb and III trials, including two drugs that are being tested for the treatment of multidrug-resistant TB (MDR-TB) (bedaquiline and delamanid), with dossiers submitted to drug regulatory authorities. One of these (bedaquiline) has recently been granted licensure by the U.S. Food and Drug Administration under its accelerated approval procedure.
- Novel drug combinations for shortened treatment of DS and/or drug-resistant (DR) TB, including new or re-purposed drugs, are under investigation.

UNMET NEEDS

- **People with drug-susceptible TB** need shorter and simpler therapy;
- **People with drug-resistant TB** need a more efficacious, fully oral, shorter, less toxic and safer therapy;
- **People living with HIV** need TB drugs with no or low drug-drug interactions with antiretrovirals;
- **People with latent TB infection** need shorter and safer therapy;
- **Children with TB** need a more child-friendly treatment.

WHY THIS GUIDANCE?

The likely introduction of new drugs or drug regimens for the treatment of DS- or DR-TB will have a series of public health implications, particularly regarding:

- the responsible use of new drugs as part of set combination regimens for the treatment of DS- or DR-TB;
- the programmatic feasibility and cost-effectiveness of newly-developed treatments;
- the capacity to monitor scaled-up use of new drugs, and conduct surveillance of drug-resistance;
- the prevention of emergence of new drug resistance.

Global TB Drug Pipeline

Discovery | Preclinical Development | Clinical Development

Lead Optimization | Preclinical Development | Phase I | Phase II | Phase III

WORKING GROUP ON NEW TB DRUGS www.newtbdrugs.org

WHO STRATEGIC ROADMAP:

Policy development for introduction of new TB drugs or regimens in countries

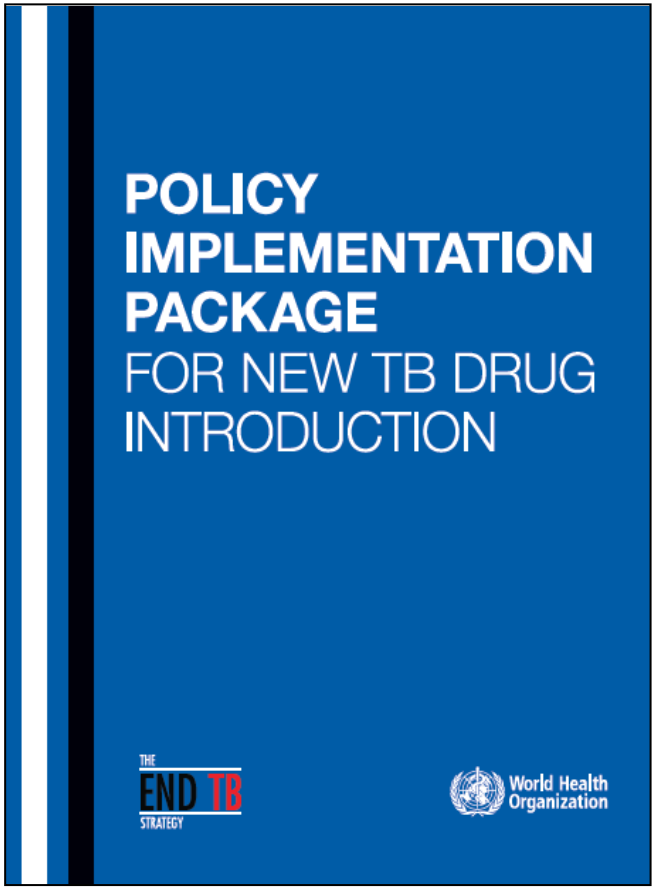
- In April 2012, the WHO Stop TB Department established a Task Force to advise and assist WHO in the process for the development of policy guidance on the rational introduction and use of new drugs or drug regimens for TB treatment. The aim is to improve access to quality TB care and to protect against the emergence of drug resistance.
- A *strategic roadmap* was then developed, with the support of the Task Force, to guide WHO's timely development of appropriate policy guidance on treatment of DS- or DR-TB and related rational introduction and use. The roadmap also includes WHO's role in supporting Member States in the roll-out of recommended new drugs within defined regimens in programmatic conditions.
- The WHO Strategic and Technical Advisory Group for Tuberculosis (STAG-TB) endorsed this roadmap in June, 2012.

SEE REVERSE FOR THE ROADMAP STEPS

For more information please visit our website:
http://www.who.int/tb/new_drugs

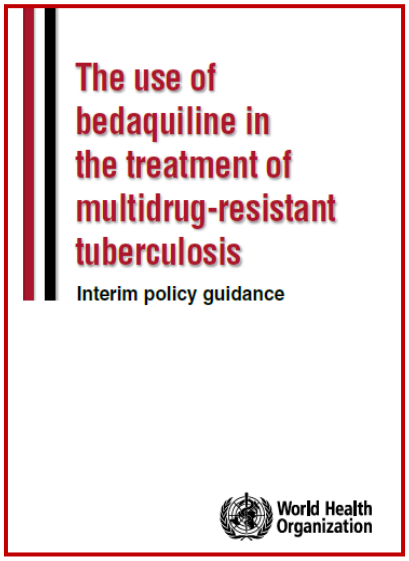
WHO Policy Implementation Package for Rational Introduction of New TB Drugs or Drug Regimens in Countries

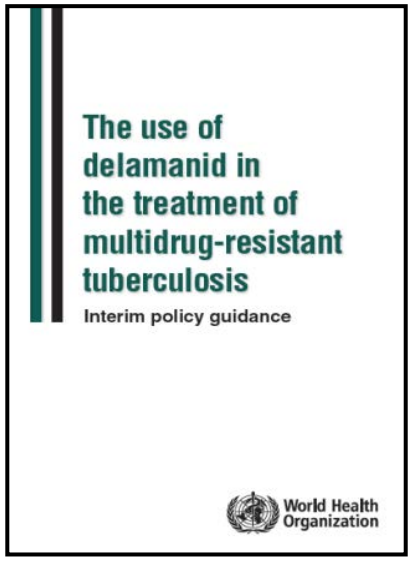
1. Minimum requirements for country preparedness and planning.
2. Implementation plan for introduction of new TB drugs or regimens.
3. Pharmacovigilance (active drug safety monitoring and management) and drug resistance surveillance.
4. Private sector engagement.
5. Systems approach for ensuring uninterrupted supply of quality-assured medicines .
6. Operational research

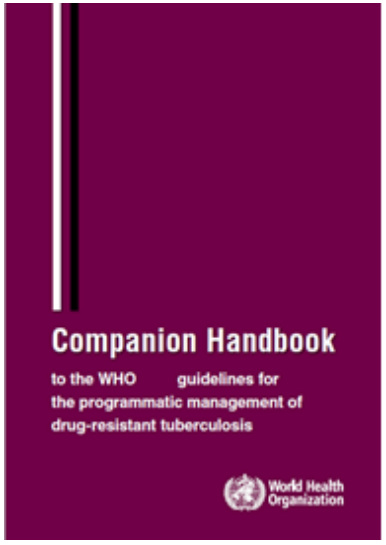


Guidance on the use of new TB drugs

- Expert consultations to evaluate new TB drugs/regimens coming out of the pipeline and revise/update treatment guidelines as appropriate
  - development of interim guidance for the use of bedaquiline
  - development of interim guidance for the use of delamanid
  - backed-up by the Companion Handbook on WHO guidelines for PMDT







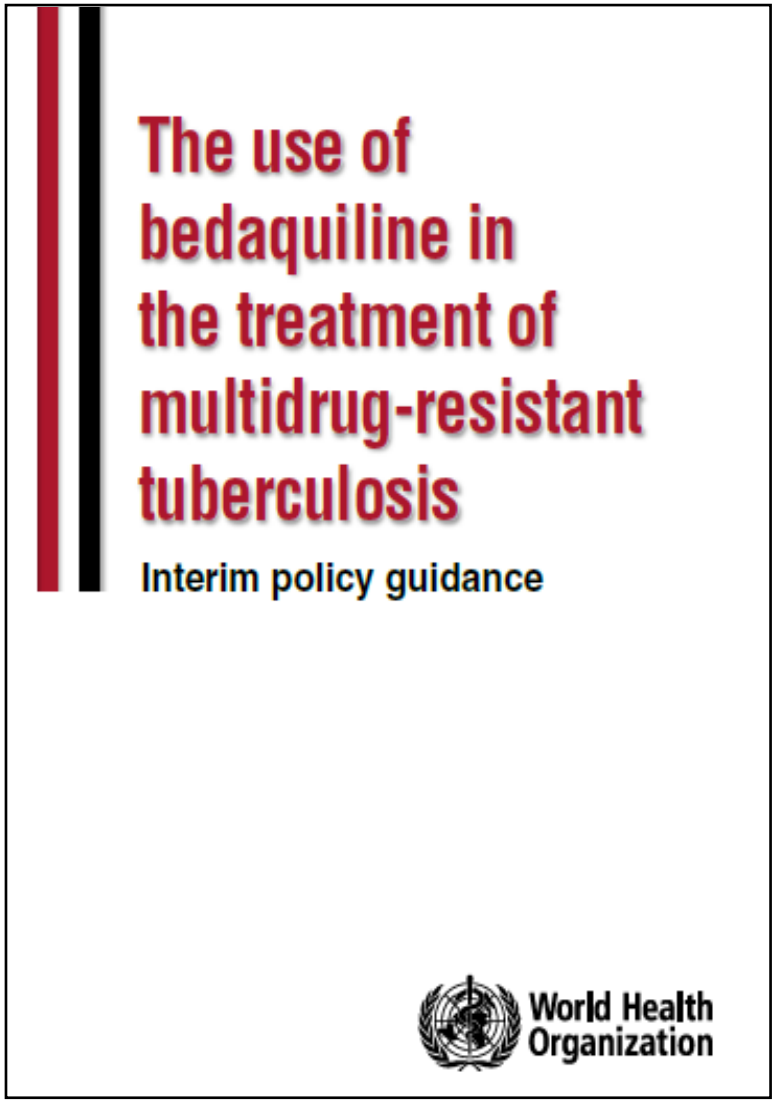
Interim policy guidance on the use of bedaquiline

"Bedaquiline may be added to a WHO-recommended regimen in adult patients with pulmonary MDR-TB, under five specific conditions"

"conditional recommendation, very low confidence in estimates of effect"

http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf?ua=1.

WHO – June 2013



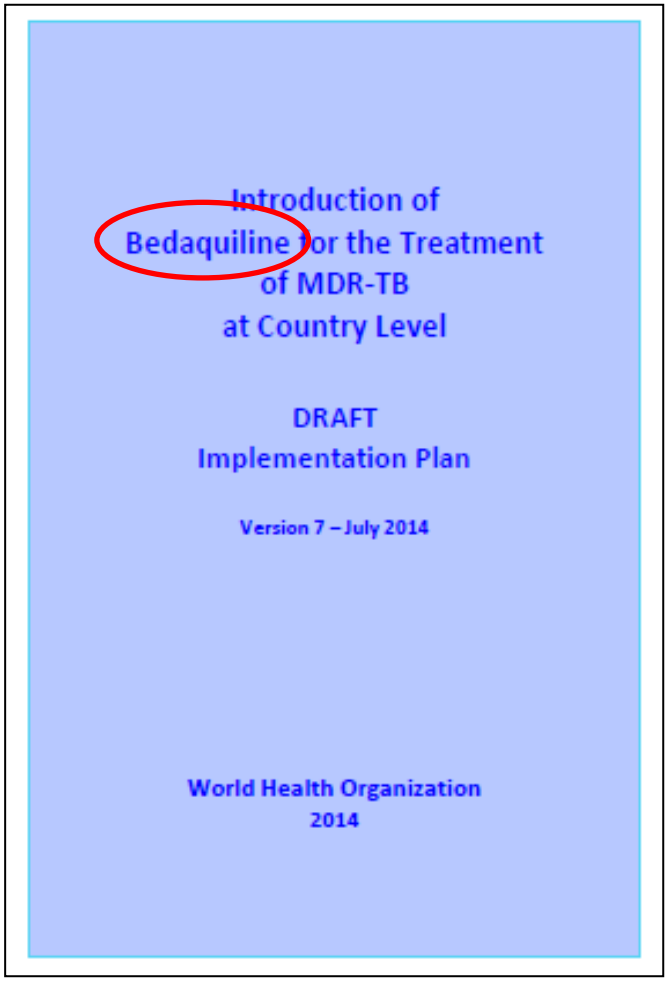
Interim policy guidance on the use of bedaquiline

5 conditions:

1. Proper selection of patients
2. Patient informed consent required
3. Treatment design based on WHO recommendations
4. Close monitoring conditions
5. Active pharmacovigilance and management of AEs

Implementation Plan for introduction of bedaquiline in countries

- Step 1: Establish the framework for the introduction of bedaquiline at country level
- Step 2: Meet the minimal requirements for introduction of bedaquiline
  - *checklist* to assist in country preparedness
- Step 3: Develop a national plan for introduction of bedaquiline
- Step 4: Implement the introduction of bedaquiline in pilot sites
- Step 5: Generate evidence for scale up



Document developed with the assistance of Marina Tadolini & Jennifer Furin

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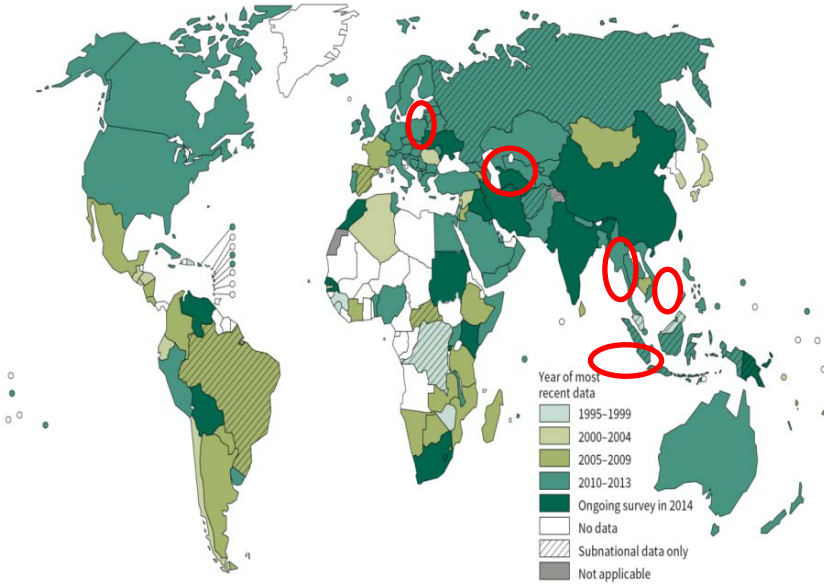
Work with 'early implementing countries'

- Countries have expressed interest in working with WHO for introduction of bedaquiline (BDQ) in programme conditions, following WHO recommendations
- Political will and funding for BDQ
- In general, high burden TB countries with
  - high rates of DR-TB
  - robust PMDT programs
  - referral centers to manage complicated patients



Work with 'early implementing countries'

- Initial **workshop** involving all key stakeholders (NTP, MoH, NRA, NPV, etc.) and TA bodies/donors (GF, USAID, B&MGF, KNCV, etc..)
  - Outline of a country-specific National Implementation Plan
  - Establishment of national framework
  - Identification of pilot sites
  - Determination of target cohort
  - Laboratory aspects
  - Monitoring – including recording and reporting
  - Establishment of plans for active drug safety management and monitoring in conjunction with key stakeholders
  - Discussion with NRAs on regulatory aspects and drug procurement
  - Timeline of activities
- Follow-up of activities at country-level

Lessons learnt (1)

- Introduction of BDQ according to WHO recommendations seems to work and countries are very much willing to do this;
- Process requires careful planning, reinforcement of some aspects/ structure (lab, R&R, M&E, PV) and training;
- Inevitable delays/hurdles and logistical challenges (e.g. high level approval, waiver for drug import, drug order approved by GF, organization of active PV, etc.)
- Long term view to improve the way new drugs are introduced: find balance given urgent needs and slow implementation process;

Lessons learnt (2)

- Model can be used for other new drugs and regimens as they become available;
- Need to streamline process for more countries and other new drugs;
- Train consultants, need to deliver updated information to donors, regulators
- Key role rGLCs to advise countries appropriately on ability to introduce new TB drugs/regimens and related activities