

# WHO treatment guidelines for drug- resistant tuberculosis

2016 update

OCTOBER 2016 REVISION

THE  
**END TB**  
STRATEGY



World Health  
Organization



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These guidelines were developed in compliance with the process for evidence gathering, assessment and formulation of recommendations, as outlined in the WHO Handbook for Guideline Development (version March 2014; available at [http://www.who.int/kms/handbook\\_2nd\\_ed.pdf](http://www.who.int/kms/handbook_2nd_ed.pdf)).

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**Annex 4.** GRADE tables

**Annex 5.** Evidence to decision tables

**Annex 6.** Summaries of unpublished data used for the recommendations

**Annexes 4, 5 and 6 are only available online at:**

[www.who.int/entity/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/](http://www.who.int/entity/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/)

# Abbreviations & acronyms<sup>1</sup>

<b>aDSM</b>	active TB drug safety monitoring and management
<b>aOR</b>	adjusted odds ratio
<b>AIDS</b>	acquired immunodeficiency syndrome
<b>aIPD</b>	adult individual patient data
<b>CDC</b>	United States Centers for Disease Control and Prevention
<b>CL</b>	confidence limits
<b>CNS</b>	central nervous system
<b>CPTR</b>	Critical Path to TB Drug Regimens
<b>DSMB</b>	Data and Safety Monitoring Board
<b>DST</b>	drug susceptibility testing
<b>EBA</b>	early bactericidal activity
<b>ERG</b>	External Review Group
<b>GDF</b>	Global Drug Facility
<b>GDG</b>	Guideline Development Group
<b>GRADE</b>	Grading of Recommendations Assessment, Development and Evaluation
<b>GRC</b>	WHO Guideline Review Committee
<b>GTB</b>	WHO Global TB Programme
<b>HIV</b>	human immunodeficiency virus
<b>IPD</b>	individual patient data
<b>KNCV</b>	KNCV Tuberculosis Foundation
<b>LSHTM</b>	London School of Hygiene and Tropical Medicine
<b>LTBI</b>	latent TB infection
<b>MDR-TB</b>	multidrug-resistant tuberculosis
<b>MIC</b>	minimum inhibitory concentration
<b>MSF</b>	Médecins sans Frontières
<b>MTBDRs/</b>	GenoType <i>Mycobacterium tuberculosis</i> drug-resistant second-line assay
<b>NTM</b>	non-tuberculous mycobacteria
<b>OR</b>	odds ratio
<b>PICO</b>	Patients, Intervention, Comparator and Outcomes
<b>pIPD</b>	paediatric individual patient data
<b>RCT</b>	randomized controlled trial
<b>RR-TB</b>	rifampicin-resistant TB
<b>SAE</b>	serious adverse event
<b>SIAPS</b>	Systems for Improved Access to Pharmaceuticals and Services
<b>TAG</b>	Treatment Action Group
<b>TB</b>	tuberculosis
<b>TB-PRACTECAL</b>	Pragmatic Clinical Trial for a More Effective Concise and Less Toxic MDR-TB Treatment Regimen(s)
<b>UNION</b>	International Union Against Tuberculosis and Lung Disease
<b>USAID</b>	United States Agency for International Development
<b>WHO</b>	World Health Organization
<b>XDR-TB</b>	extensively drug-resistant tuberculosis

<sup>1</sup> See also page 23 for the abbreviations of the names of TB medicines.

# Acknowledgements

The recommendations and remarks contained in this document resulted from the discussions of an *ad hoc* Guideline Development Group (GDG) convened by the Global TB Programme (GTB) of the World Health Organization (WHO) in Geneva, Switzerland from 9 to 11 November 2015 ([Annex 1](#)). WHO gratefully acknowledges the contributions made by this Group ahead of, during and after this meeting by its members, namely Holger Schünemann (Chair and GRADE methodologist) and Charles L Daley (Co-Chair) and other experts: Farhana Amanullah, José A Caminero, Tsira Chakhaia, Daniela Cirillo, Kelly Dooley, Luis Gustavo do Valle Bastos, Michel Gasana, Agnes Gebhard, Armen Hayrapetyan, Antonia Kwiecien, Sundari Mase, Lindsay McKenna, Nguyen Viet Nhung, Maria Rodriguez, James Seddon, Tom Shinnick, Alena Skrahina, and Carlos Torres-Duque ([Annex 2](#)). The experts on the External Review Group (ERG) who provided comments in preparation of the meeting and on the draft document before its finalization – Chen-Yuan Chiang, Dalene von Delft, Vaira Leimane, Guy Marks, Norbert Ndjeka, Lee Reichman and Rohit Sarin – are also acknowledged.

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# Declarations of interest

## Guideline Development Group (GDG)

The scope of the guidelines update, and the composition of the GDG, including their biographies, were made public for comment ahead of the meeting in line with WHO's conflict of interest policy. All GDG members completed the WHO Declaration of Interest forms. The WHO Guideline Steering Committee in preparation for the update of the guidelines and the GDG meeting reviewed the completed forms.

The following GDG members *declared no interests*: Luis Gustavo do Valle Bastos, José A Caminero, Tsira Chakhaia, Michel Gasana, Armen Hayrapetyan, Antonia Kwiecien, Sundari Mase, Nguyen Viet Nhung, Maria Rodriguez, Holger Schünemann, James Seddon and Alena Skrahina.

The following GDG members *declared interests* that were judged not to be in conflict with the objectives of the meeting:

Farhana Amanullah declared having received funding for consultancies (US\$500/day) and travel from WHO; and grants from the Global Fund and TB-REACH to cover her salary (10% full time equivalent).

Daniela Cirillo declared having received funding from FIND to conduct evaluation of drug susceptibility testing (DST) for new drugs (US\$16 000), and from Otsuka to evaluate DST for delamanid (US\$25 000). She also declared being the head of a supranational TB reference laboratory in Italy involved in country capacity building in DST technologies for second-line drugs and new diagnostics for drug-resistant TB; and being a member of the Italian national committee for the use of bedaquiline.

Charles I. Daley declared having received funding from Otsuka to serve as chair of the data

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