

WHO consolidated guidelines on tuberculosis

Module 4: Treatment

**Drug-resistant
tuberculosis treatment**



World Health
Organization

WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment

ISBN 978-92-4-000704-8 (electronic version)

ISBN 978-92-4-000705-5 (print version)

© World Health Organization 2020

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization. (<http://www.wipo.int/amc/en/mediation/rules/>)

Suggested citation. WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

Sales, rights and licensing. To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <http://www.who.int/about/licensing>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

Design by Inis Communication.

WHO consolidated guidelines on tuberculosis

Module 4: Treatment

**Drug-resistant
tuberculosis treatment**

Contents

Acknowledgements.....	iv
Abbreviations and acronyms.....	vii
Definitions.....	ix
Executive summary.....	xi
Introduction.....	1
Recommendations.....	4
Section 1. Regimen for rifampicin-susceptible, isoniazid-resistant tuberculosis.....	4
Section 2. Shorter all-oral bedaquiline-containing regimen for multidrug- or rifampicin-resistant tuberculosis.....	12
Section 3. Longer regimens for multidrug- or rifampicin-resistant tuberculosis.....	21
Section 4. The bedaquiline, pretomanid and linezolid (BPaL) regimen for multidrug-resistant tuberculosis with additional fluoroquinolone resistance.....	41
Section 5. Monitoring patient response to MDR-TB treatment using culture.....	54
Section 6. Starting antiretroviral therapy in patients on second-line antituberculosis regimens.....	58
Section 7. Surgery for patients on MDR-TB treatment.....	60
Section 8. Care and support for patients with MDR/RR-TB.....	62
Research gaps.....	72
References.....	76
Supplementary Table.....	90

Online annexes

Annex 1: Methods and expert panels

Annex 2: Declarations of interest

Annex 3: GRADE evidence summary tables

Annex 4: GRADE evidence to decision tables

Annex 5: Summaries of unpublished data

Annex 6: Statistical analysis plans

Acknowledgements

The recommendations and remarks in the current module on the treatment of drug-resistant tuberculosis (TB) are the result of collaborative efforts of professionals from a range of specialties who have extensive expertise and experience in public health policy, TB programme management, and the care and management of patients with drug-resistant TB and multidrug-resistant TB (MDR-TB). The recommendations herein have been developed through a number of meetings of the Guideline Development Group (GDG), and have then been consolidated in the present module. The World Health Organization (WHO) acknowledges and is grateful for the time and support of all individuals who have contributed to these efforts.

Recommendations for the management and care of drug-resistant tuberculosis, 2020 update

The production and writing of this document – *WHO consolidated guidelines on tuberculosis: module 4: treatment: drug-resistant tuberculosis treatment* – was coordinated by Fuad Mirzayev, with the support of Medea Gegia, Lice Y. González-Angulo, Linh Nguyen and Kerri Viney, under the guidance of Karin Weyer and Matteo Zignol, and the overall direction of Tereza Kasaeva, Director of the WHO Global TB Programme. The WHO Global TB Programme gratefully acknowledges the contribution of all experts involved in the production of these guidelines.

Guideline Development Group

The chairs of the GDG were Holger J. Schünemann (Chair, Grading of Recommendations Assessment, Development and Evaluation [GRADE] methodologist: Cochrane Canada & McMaster University, Canada) and Rafael Laniado-Laborin (Co-chair, clinician, national TB programme [NTP], end-user: NTP and Regional Green Light Committee [rGLC], Mexico). The following experts served as members of the GDG: Susan Abdel-Rahman (pharmacology, pharmacodynamics, pharmacokinetics: Children's Mercy Hospital Kansas City, United States of America [USA]); Erlina Burhan (clinician, end-user: Department of Respiratory and Pulmonology, Persahabatan Hospital, Indonesia); Daniela Cirillo (laboratory specialist: San Raffaele TB Supranational Reference Laboratory, Italy); Charles Daley (pulmonologist, MDR-TB expert: National Jewish Health, USA); Geraint Gerry Rhys Davies (trials expert, pharmacologist: University of Liverpool, United Kingdom of Great Britain and Northern Ireland [United Kingdom]); Fernanda Dockhorn Costa Johansen (NTP, end-user, clinician: Ministry of Health MDR-TB Referral Centre, Brazil); Kelly Dooley (clinical pharmacologist, researcher: Johns Hopkins University School of Medicine, USA); Bernard Fourie (clinical trials expert: University of Pretoria, South Africa); Agnes Gebhard (technical agency, end-user, clinician: KNCV Tuberculosis Foundation, Netherlands); Elmira Gurbanova (rGLC, clinician, end-user: Lung Clinic, University of Tartu, Estonia, WHO Collaborating Centre on TB in Prisons, Azerbaijan); Muhammad Amir Khan (civil society representative; Association for Social Development, Pakistan); Yuhong Liu (clinician, end-user: Clinical Center on TB, Chinese Center for Disease Control and Prevention [China CDC], Beijing Chest Hospital, WHO Collaborating Centre on TB Research and Training, China); Marian Loveday (specialist scientist, maternal health medicine: South African Medical Research Council, South Africa); Barend (Ben) Marais (paediatrician: The University of Sydney School of Medicine, Australia); Iqbal Master (clinician, MDR-TB physician, end-user: King George V Hospital, South Africa); Alberto Mendoza (clinician, end-user: NTP, Peru); Beatrice

Mutayoba (programme manager, end-user: National TB and Leprosy Programme, United Republic of Tanzania); Payam Nahid (clinician, clinical trials expert: University of California San Francisco & American Thoracic Society, USA); Mahshid Nasehi (programme manager, end-user: National TB and Leprosy Control Programme, Iran); Alberto Piubello (clinician, MDR-TB physician, end-user: International Union Against Tuberculosis and Lung Disease, Niger); Maria Rodríguez (clinician, NTP, end-user: Ministry of Health MDR-TB Referral Centre, Dominican Republic); Rohit Sarin (technical agency, end-user: National Institute of TB & Respiratory Diseases, India); Ingrid Schoeman (former MDR-TB patient: TB PROOF, South Africa); Alena Skrahina (NTP, MDR-TB physician, end-user: Republican Research and Practical Centre for Pulmonology and Tuberculosis, Belarus); Carrie Tudor (nursing specialist, technical agency, end-user: International Council of Nurses, South Africa); Debrah Vambe (NTP, end-user: NTP, Eswatini); Andrew Vernon (trials expert, technical agency, end-user: United States Centers for Disease Control and Prevention [US CDC], USA); and Nguyen Viet Nhung (NTP, end-user: NTP, Ministry of Health, Viet Nam).

External Review Group

We thank the External Review Group (ERG), which had the following members: Heather Alexander (federal agency, technical partner: International Laboratory Branch, Division of Global HIV and Tuberculosis, US CDC, USA); Giovanni Battista-Migliori (clinician, researcher: European Respiratory Society (ERS) liaison officer, ERS TB Collaborating Centre, Maugeri Institute, Italy); Anuj K. Bhatnagar (clinician, researcher: Rajan Babu Institute for Pulmonary Medicine and Tuberculosis, India); Lisa Chen (researcher: Curry International Tuberculosis Center, USA); Farhana Amanullah (paediatrician, paediatric nephrologist: Interactive Research and Development, Pakistan); Mildred Fernando-Pancho (civil society, former MDR-TB patient, Philippines); Anna Marie Celine Garfin (end-user, clinician: NTP, Philippines); Edwin H. Herrera-Flores (clinician, end-user: Hospital Nacional MDR-TB referral centre, Arzobispo Loayza, Lima, Peru); Mathilde Jachym (clinician, pneumologist: Sanatorium, France); Guy Marks (technical agency, end-user, clinician, researcher: International Union Against Tuberculosis and Lung Disease, Australia); Andrei Maryandyshev (clinician: Northern State Medical University Arkhangelsk, Russian Federation); Lawrence Mbuagbaw (epidemiologist, biostatistician: McMaster University, Canada); Thato Mosidi (civil society, former MDR-TB patient, South Africa); Bhabana Shrestha (clinician, end-user: Nepal Anti-TB Association, Nepal); Welile Sikhondze (clinician, researcher: NTP, Eswatini); Sarabjit Singh Chadha (technical agency: Global Drug Initiative Working Group, Foundation for Innovative New Diagnostics [FIND], India); Ivan Solovic (clinician, end-user: National Institute for TB, Lung Diseases and Thoracic Surgery, Slovakia); Carlos Torres (technical agency, end-user, clinician: Latin American Thoracic Society, Colombia); and Zarir Udwadia (clinician, end-user: Hinduja Hospital MDR-TB Referral Centre, Breach Candy Hospital and Parsee General Hospitals, Mumbai, India).

Evidence reviewers

WHO would also like to acknowledge the work conducted by the following evidence reviewers: Richard Menzies (lead evidence reviewer: McGill University's Faculty of Medicine, Canada); Jonathon R. Campbell (epidemiologist, health economist: McGill University's Faculty of Medicine, Canada); Amrita Daftary (behavioural health scientist: Dahdaleh Institute for Global Health Research, York University, Canada); Gabriela Gomez (health economist: London School of Hygiene and Tropical Medicine, United Kingdom); Emily Ann Kendall (assistant professor of medicine: Johns Hopkins University School of Medicine, USA); Stephanie Law (qualitative researcher: McGill University, Canada); and Rada Savic (bioengineering and pharmacokinetics/pharmacodynamics expert: University of California San Francisco, USA); and Nicholas Winters (research assistant: McGill University's Faculty of Medicine, Canada).

Observers and external partners

Draurio Barreira Cravo Neto (technical manager, TB: Unitaid, Switzerland); Dan Everitt (vice president and senior medical officer: TB Alliance, USA); Christopher Gilpin (global laboratory coordinator: International Organization for Migration, Switzerland); Anisa Hajizadeh (GRADE methods trainee: McMaster University, Canada); Brian Kaiser (technical officer: Stop TB Partnership's Global Drug Facility, Switzerland); Blessi Kumar (civil society representative: Global Coalition of TB Activists, India); Tamara Lotfi (GRADE methodologist: American University of Beirut, South Africa); YaDiul Mukadi (technical advisor: United States Agency for International Development [USAID], USA); Norbert Ndjeka (director, Drug-Resistant TB, TB & HIV: Department of Health of the Republic of South Africa, South Africa); Eugene Sun (head of Research & Development: TB Alliance, USA); Kitty Van Weezenbeek (executive director: KNCV TB Foundation, Netherlands); Francis Varaine (project lead, EndTB Project: Médecins Sans Frontières, France); and Mohammed Yassin (senior disease advisor, TB: The Global Fund to Fight AIDS, Tuberculosis and Malaria, Switzerland).

WHO Guideline Steering Committee

The following staff served as the WHO Steering Committee for the development of the current policy guideline: Fuad Mirzayev (lead), Dennis Falzon, Medea Gegia, Lice González-Angulo, Ernesto Jaramillo, Alexei Korobitsyn, Linh Nhat Nguyen, Kerri Viney, Karin Weyer, Matteo Zignol from the WHO Global TB Programme; Corinne Simone Collette Merle from the WHO Special Programme for Research and Training in Tropical Diseases; Lorenzo Moja from the WHO Medicines Selection, Intellectual Property and Affordability / Essential Medicines; Andreas Alois Reis from WHO Health Ethics and Governance; and Satvinder (Vindi) Singh from the WHO Global HIV, Hepatitis and STIs Programmes / Treatment, Care and Service Delivery. The text of the present module on treatment of drug-resistant TB was drafted by Lice González-Angulo and Kerri Viney.

Funding

USAID, Unitaid and the Russian Federation are acknowledged for their financial support to the guideline development process.

预览已结束，完整报告链接和二维码如下：

https://www.yunbaogao.cn/report/index/report?reportId=5_24539

