## **Modified 9-month all-oral regimens for MDR/RR-TB**

### Recommendation: 2.2 (new)

WHO suggests using the 9-month all-oral regimens (BLMZ, BLLfxCZ and BDLLfxZ) over currently recommended longer (>18 months) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. Amongst these regimens, using BLMZ is suggested over using BLLfxCZ, and BLLfxCZ is suggested over BDLLfxZ.

(Conditional recommendation, very low certainty of evidence)

# BLMZ BLLfxCZ BDLLfxZ

## Recommendations: 2.3 (new)

WHO suggests against using 9-month DCLLfxZ and DCMZ regimens compared with currently recommended longer (>18 months) regimens in patients with fluoroquinolone-susceptible MDR/RR-TB.

(Conditional recommendation, very low certainty of evidence)





## MDR/RR-TB regimen groups, 2025 guidelines

#### 6-month regimen - BPaLM/BPaL regimen

#### (MDR/RR-TB and pre-XDR-TB)

- in patients (aged ≥14 years) with MDR/RR-TB who have not had previous exposure to bedaquiline, pretomanid and linezolid (defined as >1 month exposure).
- This regimen may be used without moxifloxacin (BPaL) in the case of documented resistance to fluoroquinolones (in patients with pre-XDR-TB).
- DST to fluoroquinolones is strongly encouraged, but DST should not delay treatment initiation.
- Cannot be used during pregnancy
- People with all forms of extrapulmonary TB except for TB involving the CNS, osteoarticular, or disseminated forms of TB with multiorgan involvement.

#### 6-month BDLLfxC

#### MDR/RR-TB and pre-XDR-TB

- People with MDR/RR-TB or pre-XDR-TB
- People with MDR/RR-TB and less than one month of previous exposure to bedaquiline, linezolid, delamanid, or clofazimine.
- People with diagnosed pulmonary TB, including children, adolescents, PLHIV, pregnant and breastfeeding women.
- People with all forms of extrapulmonary TB except for TB involving the CNS, osteoarticular, or disseminated forms of TB with multiorgan involvement.

#### Modified 9-month regimens

#### MDR/RR-TB

- People with MDR/RR-TB and without resistance to fluoroquinolones;
- People with diagnosed pulmonary TB, including children, adolescents, PLHIV, pregnant and breastfeeding women.
- People with extensive TB disease and all forms of extrapulmonary TB except for TB involving the CNS,
- for TB involving the CNS, osteoarticular, or disseminated forms of TB with multi-organ involvement.
- People with MDR/RR-TB and less than one month of previous exposure to bedaquiline, fluoroquinolones, linezolid, and clofazimine

## 9-month regimen (MDR/RR-TB)

#### ....., .... . . . ,

- 2 months of linezolid (600 mg) can be used as an alternative to 4 months of ethionamide.
- no previous exposure to second-line treatment (including bedaquiline),
- no fluoroquinolone resistance and no extensive pulmonary TB disease
- or severe extrapulmonary TB.
   rapid DST for ruling out
- fluoroquinolone resistance is required.
- can be used in all age groups
   regimen with linezolid can be used in pregnant women

## 18-month - longer regimens, individualized, mostly in XDR-TB)

- Last resort regimen
- Those who failed or not eligible for two shorter regimens
- XDR-TB patients
- Individualized based on current recommendations

6-month

9-month

18-month





## **Implementation challenges with the new regimens**

- ✓ Diagnostic barriers
- ✓ High price of some medicines
- ✓ Medicines availability and procurement
- ✓ Programmatic implementation barriers:
  - previous regimens in use,
  - innovation doubts,
  - regulatory barriers,
  - policy updates or local research





## **Expected new evidence from treatment trials\***

### End-stage trials on DR-TB treatment

Next-TB, MDR-End, Stream 1 and 2	Nix, ZeNix	TB PRACTECAL, endTB, BEAT- Tuberculosis	endTB Q
Trials that used de- recommended SoC as comparator or already recommended intervention – important contribution to the knowledge on TB but cannot be used for new policy	no comparator, contributing to the knowledge and supporting regulatory approval but challenge to match the policy development process	Contributed to the policy development	only phase 3 trial that may contribute to the policy in the next couple of years, depending on the results

A wave of phase 2 trials is ongoing and may contribute new products for further research under phase 3 trials in the next 5 years











\*not including host-directed therapies or stratified medicine



## **Main messages**

- Shorter, 6-month BPaLM/BPaL is the preferred choice for patients with MDR/RR-TB or pre-XDR-TB above 14 years of age
- 6-month BDLLfxC is a 6-month alternative for those not eligible for BPaLM, and it can be used in all patients (including children and pregnant women)
- Modified 9-month regimens can also be used for patients with MDR-RR-TB (but no FQ resistance), adding a choice of regimens with fewer component medicines to the group of 9-month regimens (including currently recommended)
- Longer, 18-20 months regimens remain the "last resort" individualized regimens
- The duration of MDR/RR-TB treatment can be the same as DS-TB treatment for most patients, including children and during pregnancy.





- In 2025 consolidation of several guidelines and handbooks in Module 4: Treatment
- DS-TB: 3 regimens, two shorter, 4-month regimens for and 6-month regimen remains recommended
- DR-TB: 7 shorter treatment regimens 6-month BPaLM/BPaL and BDLLfxC, 3 new modified 9-month regimens and 2 previously recommended 9-month regimens
- Longer, 18-20 months regimens the "last resort" individualized regimens

