Recommendation 1.1 – The 6-month BPaLM regimen

Recommendation 1.1

WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM) rather than the 9-month or longer (18-month) regimens in MDR/RR-TB or pre-XDR TB patients.

(*Conditional recommendation, very low certainty of evidence)*

Remarks

- DST for fluoroquinolones is strongly encouraged in people with MDR/ RR-TB, and although it should not delay initiation of the BPaLM, results of the test should guide the decision on whether moxifloxacin can be retained or should be dropped from the regimen – in cases of documented resistance to fluoroquinolones, BPaL without moxifloxacin would be initiated or continued.
- This recommendation does not apply to pregnant and breastfeeding women owing to limited evidence on the safety of pretomanid.
- The recommended dose of linezolid is 600 mg once daily for BPaLM/BPaL

MDR/RR-TB regimen groups, 2022 guidelines

Clinical trials reviewed during 2024 GDG

Comparator

BEAT-TB trial in South Africa: 6-month regimen

MDR/RR-TB or pre-XDR-TB

6m Bdq-Dlm-Lzd-Lfx/Cfz/both

- Recommended 9-month regimen (with Lzd) for Fq-susceptible
- Longer regimens for Fq-resistant

EndTB trial multicountry: 9-month regimens

MDR/RR-TB

1. Bdq-Lzd-Mfx-Z
2. Bdq-Lzd-Cfz-Lfx-Z
3. Bdq-Lzd-Dlm-Lfx-Z
4. Dlm-Cfz-Lzd-Lfx-Z
5. Dlm-Cfz-Mfx-Z

Recommended longer regimens

World Health Organization

PICO 1 – BEAT-TB trial

Should a 6-month regimen using bedaquiline, delamanid, and linezolid with or without the addition of levofloxacin or clofazimine or both (BDLL/C) be used in patients with pulmonary RR-TB (with or without fluoroquinolone resistance) over the currently recommended 9-month regimen?

Population	**Intervention**	**Comparator**	**Outcome**
Patients with microbiologically confirmed pulmonary MDR/RR-TB and with or without FQ resistance	BDLLfx/C regimen[a]: **6 Bdq-Dlm-Lzd-Lfx/Cfz (and/or)**	BEAT-Tuberculosis comparator regimens: • **9 Bdq(6)-Lzd(2)-Lfx-Cfz-Hh-Z-E (for Fq-susceptible)** • **WHO currently recommended longer regimens (18-20 months) (for Fq-resistant)**	• Sustained treatment success • Failure and recurrence • Death • Lost to follow up • Adverse events • Amplification (acquisition) of drug resistance

Recommendation 1.2 – The 6-month BDLLfxC regimen

Recommendation 1.2 (new)

WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance.

(Conditional recommendation, very low certainty of evidence).

Remarks

1. When resistance to fluoroquinolones is unknown, the regimen can be started as BDLLfxC and then adjusted based on the DST results. In cases of quinolone susceptibility, the regimen can include four medicines— bedaquiline, delamanid, linezolid and levofloxacin (BDLLfx). In cases of resistance to fluoroquinolones, the regimen with bedaquiline, delamanid, linezolid and clofazimine (BDLC) can be used.
2. During the randomized controlled trial, the BDLLfxC regimen group was compared to the group of participants who received either a previously recommended 9-month shorter regimen with linezolid or the longer(>18 months) WHO-recommended regimens. The majority of controls were on the 9-month regimen.

PICO 2 – endTB trial

Should any 9-month endTB trial regimens be used in patients with pulmonary RR-TB (without fluoroquinolone resistance) over the currently recommended longer regimens?

Population	Intervention	Comparator	Outcome
Patients with microbiologically confirmed pulmonary MDR/RR-TB and without FQ resistance	endTB 1 regimen[a]: **9 Bdq-Lzd-Mfx-Z** endTB 2 regimen[b]: **9 Bdq-Lzd-Cfz-Lfx-Z** endTB 3 regimen[c]: **9 Bdq-Lzd-Dlm-Lfx-Z** endTB 4 regimen[d]: **9 Dlm-Cfz-Lzd-Lfx-Z** endTB 5 regimen[e]: **9 Dlm-Cfz-Mfx-Z**	**WHO currently recommended longer regimens (18-20 months)**	• Sustained treatment success • Failure and recurrence • Death • Lost to follow up • Adverse events • Amplification (acquisition) of drug resistance