Tuberculosis Treatment: Drug-Susceptible & Drug-Resistant

4-month rifapentine-moxifloxacin and pediatric regimens for drug-susceptible TB; 6-month BPaL/BPaLM regimens for rifampin-resistant TB, replacing ≥15-month standard therapy.

2025 ATS/CDC/ERS/IDSA Clinical Practice Guideline
Treatment of Drug-Susceptible Tuberculosis & Novel Treatment Regimens for RR-TB
Saukkonen, Duarte, Munsiff et al. · Am J Respir Crit Care Med 2025;211(1):15-33

FORMAT *4 GRADE PICO recommendations. RR = rifampin-resistant; FQ = fluoroquinolone; DOT = directly observed therapy.*

1 Q1 — Drug-Susceptible TB, Adults & Adolescents ≥12 y

STATEMENT	STRENGTH
Rec — In people ≥12 y with DS pulmonary TB, use a 4-month regimen of isoniazid + rifapentine + moxifloxacin + pyrazinamide (2HPZM/2HPM) rather than the standard 6-month 2HRZE/4HR	Conditional Moderate

Noninferior to 6-mo regimen (84.6% vs. 85.4% cure). Avoids ethambutol ocular toxicity; higher daily pill burden. Screen for FQ resistance (molecular ± phenotypic) before starting. Not studied in EPTB (CNS, bone/joint, miliary, pericardial) — use standard regimen for those.

2 Q2 — Nonsevere DS-TB, Children & Adolescents 3 mo–16 y

STATEMENT	STRENGTH
Rec — In children/adolescents 3 mo–16 y with nonsevere TB (no suspicion/evidence of MDR/RR-TB), use a 4-month regimen 2HRZ(E)/2HR rather than 6-month 2HRZE/4HR	Strong Moderate

Nonsevere TB = peripheral LN TB; intrathoracic LN TB w/o airway obstruction; uncomplicated pleural effusion; or paucibacillary, noncavitary disease confined to one lobe without a miliary pattern. Not meeting criteria → standard 6-mo regimen or EPTB-specific regimen. Some may also qualify for the adult 4-mo RPT-MOX regimen.

3 Q3 — RR-TB, Fluoroquinolone-Resistant, Age ≥14 y

STATEMENT	STRENGTH
Rec — RR pulmonary TB with FQ resistance/intolerance, and no prior bedaquiline/linezolid exposure (or <1 mo exposure): use 6-month BPaL rather than ≥15-month regimens	Strong Very low

BPaL = bedaquiline + pretomanid + linezolid. Excluded from trial evidence: pregnancy/lactation, age <14 y, severe EPTB (CNS, bone/joint, miliary, pericardial). If ineligible, consider an individualized regimen per the 2019 DR-TB guideline.

4 Q4 — RR-TB, Fluoroquinolone-Susceptible, Age ≥14 y

STATEMENT	STRENGTH
Rec — RR, FQ-susceptible pulmonary TB: use 6-month BPaLM rather than ≥15-month regimens	Strong Very low

BPaLM = BPaL + moxifloxacin. TB-PRACTECAL: 89% vs. 52% treatment success, less failure/recurrence, less loss to follow-up, fewer grade 3–5 AEs than standard of care. Same exclusions as Q3 apply (severe EPTB, pregnancy, age <14 y).

5 Recommended Regimen Dosing

REGIMEN	DOSING
4-mo HPZM (Q1)	Isoniazid 300 mg/d + rifapentine 1,200 mg/d + moxifloxacin 400 mg/d × 17 wk; pyrazinamide (wt-based: 1,000–2,000 mg/d) intensive phase only, 8 wk. + Pyridoxine 25–50 mg/d throughout
Standard 6-mo 2HRZE/4HR	Isoniazid 5 mg/kg + rifampin 10 mg/kg + pyrazinamide 25 mg/kg + ethambutol 15–20 mg/kg × 2 mo, then isoniazid + rifampin × 4 mo
4-mo children 2HRZ(E)/2HR (Q2)	WHO wt-based: isoniazid 10–15 mg/kg, rifampin 10–20 mg/kg, pyrazinamide 35 (30–40) mg/kg, ± ethambutol 20 (15–25) mg/kg × 8 wk, then isoniazid + rifampin × 8 wk
BPaL (Q3, 26 wk)	Bedaquiline 400 mg/d × 2 wk then 200 mg 3×/wk × 24 wk; pretomanid 200 mg/d × 26 wk; linezolid 600 mg/d × 26 wk
BPaLM (Q4, 26 wk)	As BPaL, plus moxifloxacin 400 mg/d × 26 wk. All regimens: DOT ≥5/7 d per week; take with food, avoiding milk/antacids/cationic agents

6 BPaL / BPaLM — Key Exclusions & Cautions

FACTOR	CONSIDERATION
Age < 14 y	Insufficient safety/efficacy data — use longer standard regimens per 2019 DR-TB guidance
Pregnancy / lactation	Excluded from all trials — avoid until safety data available
Prior BDQ/LZD exposure ≥1 mo	Not covered by this recommendation — individualize regimen selection
Severe EPTB	CNS, bone/joint, miliary, and disseminated/pericardial TB excluded from trials — no BPaL/BPaLM evidence base
Drug interactions	Avoid efavirenz (↓ bedaquiline levels), QTc-prolonging agents, strong CYP3A4 inducers/inhibitors, MAOIs, myelosuppressive drugs

7 BPaL / BPaLM — Monitoring Essentials

PARAMETER	SCHEDULE
CBC	Baseline, then q1–2wk × 6–8 wk, then monthly while on linezolid — Hgb drop >10% at wk 4 flags high anemia risk
ECG / QTc	Baseline, 2, 12, 24 wk while on bedaquiline; increase to monthly if a concomitant QT-prolonging agent (e.g., moxifloxacin) is used
Vision & neuropathy	Visual acuity/color discrimination + peripheral neuropathy exam — baseline and monthly while on linezolid
Renal / hepatic panel	Creatinine, ALT/AST/alk phos/bilirubin, K^+/Ca^{2+}/Mg^{2+}/bicarbonate — baseline and monthly
Sputum smear/culture + DST	Baseline, then q1–2wk until smear conversion, biweekly until culture conversion, then monthly through treatment
Linezolid TDM	Trough concentration after 1–2 wk of therapy where available — goal <2 µg/mL to minimize toxicity
Post-treatment	Clinical, sputum, and imaging follow-up at 3, 6, 12, 18, 24 mo to identify recurrence

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