Accelerating Progress Towards Ending TB in the African Region

Drug-resistant TB
Treatment and care

WHO Operational Handbook on Tuberculosis — Module 4: Treatment and care, second edition (2026)

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Department for HIV, TB, Hepatitis and STIs | 2026

Second edition — 2026 update

The 2026 second edition of the operational handbook

The second edition of the operational handbook on TB treatment updates and consolidates all chapters on TB treatment and care, including updates to DR-TB treatment and a new section on palliative care into a single operational resource

Chapter 2
Drug-resistant TB treatment

- ★ 6-month regimens (BPaL/M/C; BDLLfxC) — **updated 2026**
- 9-month regimens
- Longer (individualized) regimens
- Hr-TB, monitoring, adjuncts
- Programmatic implementation

Chapter 3
TB care and support

- Care and support interventions
- Models of care for DR-TB
- ★ **Palliative care for MDR/RR-TB**

★ **2026 update: 4 new recommendations on pre-XDR-TB regimens + first palliative care recommendation for DR-TB**

Understanding DR-TB — Definitions and eligibility

Accurate classification of drug-resistance patterns drives regimen decisions

DR-TB classification hierarchy

MDR/RR-TB

Resistance to **rifampicin** (with or without isoniazid resistance)

pre-XDR-TB

MDR/RR-TB + resistance to **≥1 fluoroquinolone** (levofloxacin or moxifloxacin)

XDR-TB

MDR/RR-TB + resistance to **≥1 FQ** AND **≥1 other Group A drug** (bedaquiline or linezolid)

Hr-TB

Rifampicin-susceptible, **isoniazid-resistant** TB — distinct pathway from MDR/RR-TB

Key eligibility factors for regimen selection

Assess ALL factors before choosing a regimen

FQ DST result
Known vs. unknown — determines BPaLM vs. BDLLfxC pathway

Pulmonary disease severity
Cavitation on CXR + sputum smear load (distinguishes BPaL vs. BPaLC for pre-XDR-TB)

Age
≥14 years vs. <14 years — BPaL/M/C restricted to ≥14

Pregnancy / breastfeeding
BPaLM contraindicated — route to BDLLfxC family

Prior drug exposure
<1 month vs. >1 month of second-line drug use

Extent and type of disease
Pulmonary vs. extrapulmonary (CNS/osteoarticular excluded from short regimens)

Treatment regimen options — Age ≥14 Years

Adults & older adolescents

FQ susceptibility	Severity of pulmonary disease	Preferred Regimen	Alternative Regimen
FQ Unknown	N/A	BPaLM*	BDLLfxC
FQ Susceptible	N/A	BPaLM	BDLLfx / 9-month regimens
FQ Resistant (pre-XDR-TB)	Non-Severe	BPaL	BDLC
	Severe	BPaLC	Longer regimen

* Initial regimen — adjust based on FQ susceptibility and severity once available

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Treatment regimen options — Age <14 Years

Children & young adolescents

FQ susceptibility (patient or source case)	Severity of pulmonary disease	Preferred Regimen	Alternative Regimen
FQ Unknown	N/A	BDLLfxC*	
FQ Susceptible	N/A	BDLLfx	9-month regimens (any)
FQ Resistant (pre-XDR-TB)	Non-Severe	BDLC	Longer regimen
	Severe	Longer regimen	

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* Initial regimen — adjust based on FQ susceptibility and severity once available | Note: BPaL regimens NOT recommended in <14 years

The 6-month BPaL/M/C regimen

BPaLM is the preferred first-line option for MDR/RR-TB — new 2026 sub-recommendations tailor the regimen for pre-XDR-TB by disease severity

Drug doses — BPaL/M/C components

Drug	Dose & schedule	Notes
Bedaquiline (B)	400 mg daily × 2 wk, then 200 mg 3×/wk	Alt: 200 mg daily × 8 wk, then 100 mg daily
Pretomanid (Pa)	200 mg once daily	All regimen variants
Linezolid (L)	600 mg once daily	Monitor for AEs; dose reduction protocol
Moxifloxacin (M)	400 mg once daily	Drop if FQ-resistant (BPaL only)
Clofazimine (C)	100 mg once daily	Added for severe pre-XDR-TB (BPaLC)

Duration: 26 weeks (6 months) — extendable to 39 weeks (9 months) if no bacteriological/clinical response by month 4

Recommendation B1.1 — updated 2026

B1.1 **BPaLM** — MDR/RR-TB, adults and adolescents ≥14 yrs (FQ-susceptible)

B1.1a NEW **BPaL** — Non-severe pulmonary pre-XDR-TB

B1.1b NEW **BPaLC** — Severe pulmonary pre-XDR-TB (≥14 yrs)

Severity-driven regimen selection — pre-XDR-TB

NON-SEVERE

No cavitation + smear <1+ , or smear <2+ without cavitation

→ **BPaL (6 months)**

SEVERE

Cavitation + smear ≥1+ OR smear ≥2+ (even without cavitation)

→ **BPaLC (6 months)**

Not recommended for:

- Pregnancy / breastfeeding
- CNS TB
- Osteoarticular TB
- Disseminated TB
- Age <14 years

The 6-month BDLLfx/C regimen

BDLLfx/C is the alternative for people ineligible for BPaLM — flexibility across age groups and pregnancy

Recommendation B1.2
Updated 2026 — BDLLfxC for MDR/RR-TB with or without FQ resistance

Eligible populations

- All ages incl. **children**
- **Adolescents** and adults
- **PLHIV**
- **Pregnant** and breastfeeding women

Duration

6 months (24 weeks)

Extend to **9 months** (36 weeks) if slow response or positive cultures at month 4–5

⚠ Higher cost than BPaLM due to delamanid

DST-driven regimen selection

MDR/RR-TB Patient
Start BDLLfxC → adjust on DST result

FQ status unknown → **BDLLfxC**
Start empirically; adjust on DST results
Bdq Dlm Lfx Lzd Cfz

FQ susceptible → **BDLLfx**
Drop clofazimine
Bdq Dlm Lfx Lzd Cfz

FQ resistant (pre-XDR) → **BDLC**
Drop levofloxacin (non-severe only)
Bdq Dlm Lfx Lzd Cfz

2026 pre-XDR-TB sub-recommendations

B1.2a NEW
Non-severe pulmonary pre-XDR-TB
BDLC recommended — no cavitation or low smear burden

B1.2b NEW
Severe pulmonary pre-XDR-TB
BDLC NOT recommended — use BPaLC (≥14 yrs) or longer regimen (<14 yrs)

9-month and longer regimens — when and which

Modified 9-month regimens offer a strong alternative when 6-month options are unsuitable; longer regimens remain the safety net for complex cases

Regimen	Target population	Key conditions / notes
9-month (Eto or Lzd variation) **Rec B2.1**	MDR/RR-TB, FQ-susceptible	No extensive disease; <1 month prior second-line drug exposure
Modified 9-month (BLMZ, BLLfxCZ, BDLLfxZ) **Rec B2.2–B2.3**	MDR/RR-TB, FQ-susceptible; all ages	Extensive disease OK (excludes CNS/osteoarticular/disseminated TB)
Longer regimen (18–20 months) **Rec B3.1–B3.17**	XDR-TB; failed shorter regimens	Group A + B agents; individualized composition

Modified 9-month preference order

BLMZ > BLLfxCZ > BDLLfxZ

Longer regimen core principle

All 3 Group A agents + ≥1 Group B agent at start; Group C added if needed

Longer regimen duration

15–17 months after culture conversion for most patients

Defining severity in pre-XDR-TB

Severity definition based on chest X-ray cavitation and sputum smear load — to inform the choice of pre-XDR-TB regimen

Scope of these severity definitions (B1.1a/b, B1.2a/b): pulmonary pre-XDR-TB only

General definition on advanced disease applies to **all TB** , including extrapulmonary

Patients with CNS, osteoarticular, or disseminated TB: NOT eligible for 6-month regimens — use individualized longer regimens

Pre-XDR-TB = MDR/RR-TB + resistance to ≥1 fluoroquinolone — severity classification determines the correct 6-month regimen

Severe — either criterion

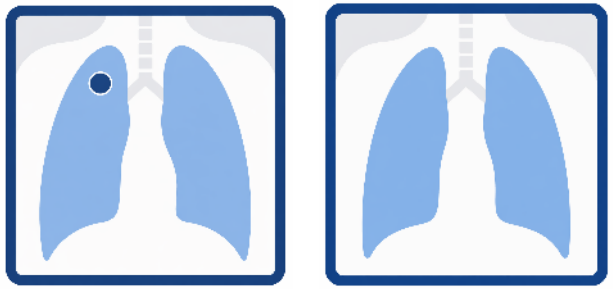
Criterion A — Cavitation + smear

- **Cavitary lesions on CXR AND sputum smear ≥1+ positivity**

OR

Criterion B — Smear alone

- Smear ≥2+ (or equivalent mWRD) even without cavitation



+ Smear ≥1+

+ Smear ≥2+

Non-Severe

Definition

- All situations **not** meeting the severe criteria

Examples

- Cavitation on CXR but smear scanty
- Smear 1+ with no cavitation

Treatment — Severe pre-XDR-TB

≥14 yrs	**BPaLC or longer regimen**
<14 yrs	**Longer regimen** — individualized

Treatment — Non-severe pre-XDR-TB

≥14 yrs	**BPaL or BDLC**
<14 yrs	**BDLC** (or longer regimen)

Special consideration — children <10 years

Severe disease includes: extensive intrathoracic lymph node disease with airway obstruction, cavitary disease, or severe respiratory compromise without cavitation

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Treatment monitoring — response and safety

Monthly bacteriological monitoring with systematic safety surveillance: backbone of MDR/RR-TB management

Response monitoring

Monthly: sputum smear + culture
Throughout entire treatment duration — primary bacteriological response indicator

Monthly: clinical assessment
Weight / BMI tracking; symptom resolution review

Month 4: key decision point
No culture conversion

Consider regimen extension or change

Radiology — PRN only
Reassess only if clinically indicated; FQ DST must NOT delay treatment start

End of treatment + 6 & 12 months post-Tx
Smear, culture, full clinical review

High-risk groups — closer monitoring required

Older adults | PLHIV | Hep B/C | Diabetes | Renal impairment | Hepatic impairment | Baseline anaemia

Safety monitoring schedule

Timepoint	Tests required
Baseline	CBC, LFTs, ECG, renal function, peripheral neuropathy screen
Week 2 (Lzd-containing)	Repeat CBC, LFTs, ECG, renal function; peripheral neuropathy screen
Monthly	Sputum smear + culture; clinical evaluation; weight; symptom review
Month 4	Bacteriological assessment — culture conversion status. If no conversion: assess for extension or change
End of Treatment	Sputum smear + culture; clinical review; LFTs if indicated
6 Months Post-Tx	Sputum smear + culture; clinical review
12 Months Post-Tx	Sputum smear + culture; clinical review; confirm durable cure

Post-treatment follow-up: Minimum 12 months after successful completion required to confirm sustained cure

Managing adverse events

Linezolid drives most clinically significant toxicity in shorter DR-TB regimens — a structured, graded management approach preserves patient safety and treatment continuity

Linezolid (Lzd)

Most toxic agent in BPaL-based regimens

Key adverse events

Myelosuppression **Peripheral neuropathy** **Optic neuropathy**

- Anaemia, neutropenia, thrombocytopenia — Grade 3+ AEs ~20% at 600 mg/day (ZeNix/TB-PRACTECAL)

Management ladder

Wks 1–9	Maintain 600 mg; permanent discontinuation in this window = stop entire regimen
Wks 9–18	Reduce to 300 mg or resume 600 mg as tolerated
Wks 18–26	May omit Lzd; restart at 300/600 mg when possible

Bedaquiline + Moxifloxacin

Cardiac monitoring required

Key adverse event

QTc prolongation

- Do not initiate if QTcF >500 ms at baseline
- ECG monitoring essential throughout treatment
- Monitor at baseline, week 2, then monthly

Additive QT risk when Bdq + Mfx combined — review ECG at each visit

Active TB drug-safety monitoring

aDSM — Mandatory framework

Mandatory for all patients on BPaL/M/C and BDLLfxC

Report serious AEs to national pharmacovigilance authority

Structured case-level reporting at baseline, monthly, end of treatment

Pyrazinamide

9-month regimens only

Key adverse event

Hepatotoxicity

- Monitor LFTs at baseline and regularly during treatment
- May discontinue if severe hepatotoxicity — without compromising efficacy

Regimen costs — BPaL/M/C vs BDLLfx/C

Cost of second-line DR-TB regimens based on GDF catalogue prices (6-month adult course, GDF EXW prices in USD, valid through December 2026)

BPaL/M/C
MDR/RR-TB and pre-XDR-TB (≥14 years)

Drug	Dose	Qty (6 mo)	Unit Price	Cost
B Bedaquiline	400 mg×2wk, 200 mg 3×/wk	~128 tabs (100 mg)	$0.49/tab	$63
Pa Pretomanid	200 mg once daily	182 tabs (200 mg)	$0.929/tab	$169
L Linezolid	600 mg once daily	182 tabs (600 mg)	$0.16/tab	$29
M Moxifloxacin	400 mg once daily	182 tabs (400 mg)	$0.143/tab	$26
C Clofazimine	100 mg once daily	182 caps (100 mg)	$0.50/cap	$91
BPaL total				**~$261**
BPaLM total				**~$287**
BPaLC total				**~$352**

BDLLfx/C
MDR/RR-TB and pre-XDR-TB; suitable for all ages including pregnancy

Drug	Dose	Qty (6 mo)	Unit Price	Cost
B Bedaquiline	400 mg×2wk, 200 mg 3×/wk	~128 tabs (100 mg)	$0.49/tab	$63
D Delamanid	100 mg twice daily	364 tabs (50 mg)	$1.77/tab	$645
L Linezolid	600 mg once daily	182 tabs (600 mg)	$0.16/tab	$29
Lfx Levofloxacin	750 mg once daily	182 tabs (750 mg)	$0.104/tab	$19
C Clofazimine	100 mg once daily	182 caps (100 mg)	$0.50/cap	$91
BDLLfxC total (adult)				**~$847**
BDLLfx total (adult)				**~$756**
BDLLfxC total (child ~15 kg)				***~$444***

D For BDLLfx/C, delamanid is the main cost driver, accounting for ~76% of the total regimen cost

Standard adult doses applied for a 26-week (182-day) treatment course. Costs shown for medicines only; ancillary costs not included.

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Programmatic implementation — getting systems ready

Successful scale-up of new DR-TB regimens requires NTPs to modernize policy, diagnostics, training, and supply chains in parallel

1 Policy & regulation

- Update national guidelines & essential medicines list
- Update DST algorithms
- Drug registration: pretomanid, clofazimine

2 National expert committee / consilium

- Coordinate regimen introduction: public & private sectors
- Provide clinical advisory support
- Oversee aDSM training

3 Laboratory capacity

- FQ DST — mandatory before 9-month regimens
- Bdq + Lzd DST for treatment failures
- WGS where available

4 Supply chain

- Quantify medicine needs by patient group
- Use GDF/rGLC technical assistance
- Child-friendly formulations; stock-out early warning

5 Electronic recording & reporting

- Capture DST patterns, regimen type, outcomes
- Digital tools (e.g. QuanTB) for forecasting
- Link to national pharmacovigilance (aDSM)

Overarching principle: *Person-centred care and social support are integral to any regimen — not add-ons*

Palliative care — a new WHO recommendation for DR-TB

For the first time, WHO explicitly recommends integrating palliative care into MDR/RR-TB treatment — a milestone in comprehensive, person-centred TB care

New 2026

Recommendation C4.1

"In patients with pulmonary MDR/RR-TB, in addition to effective treatment, WHO recommends integrating palliative care assessment and interventions by trained providers, as described in WHO palliative care guidance documents."

Conditional recommendation, moderate certainty of evidence

Evidence base

Nurse-led palliative care RCT, Uganda (Buyinza N et al., Lancet Global Health 2025)

Structured palliative care package (social, nutritional, psychological, spiritual, symptom-relief) alongside TB treatment vs. effective TB treatment alone — at 4 months.

Key trial results at 4 months

+3.84 improvement
WHOQoL psychological domain score
Effect size: 1.01 — Large

+2.32 improvement
WHOQoL social domain score
Effect size: 0.84 — Large

−4.52
Psychological distress (GHQ-12 scale)
$p < 0.0001$

93% vs. 56%
Treatment adherence — palliative care vs. control
OR 10.77, $p < 0.0001$

Other appropriately trained providers may deliver this care. Also applicable to selected DS-TB patients with high palliative care needs following assessment

What does palliative care for DR-TB look like?

Palliative care for DR-TB is a structured, multi-domain package — delivered at every level of the health system, by trained providers, from diagnosis through survivorship

When

Initiate at diagnosis based on needs assessment; continue through and beyond treatment (post-TB lung disease, long-term impairment)

Where

TB hospitals · District hospitals · Primary health centers · Patient homes

Who provides care

TB physicians · Primary care nurses (30–40 hrs palliative care training) · Community health workers · Social workers · Psychologists

Specialist palliative care for refractory cases

Physical

- Pain relief (non-opioid and opioid)
- Dyspnoea management (oxygen, bronchodilators)
- Cough suppression & diarrhoea management
- Adverse event symptom relief

Psychological / emotional

- Screening for depression and anxiety
- Psychological support & counselling
- End-of-treatment counselling
- Support for post-TB sequelae

Social

- Material support: food, transport, financial
- Educational support & accompaniment
- Peer support networks
- Address stigma and discrimination

Spiritual

- Spiritual care based on patient beliefs and preferences
- Individualized to cultural context
- Delivered by appropriately trained providers

Integrating palliative care into national TB programmes

NTPs must take the lead where palliative care services are absent — formal integration into TB programme structures is the path to sustainable impact at scale

Define the essential package

List palliative care interventions: medicines, equipment, social supports, human resources

Ensure medicine access

Regulatory access to essential palliative care medicines, including opioids

National collaboration

Establish official linkages between existing national palliative care programs and the NTP to align resources and avoid duplication.

Estimate patient numbers

Quantify the population to be served to plan capacity and procurement

Set up M&E indicators

Monitoring and evaluation indicators specific to palliative care outcomes

Post-TB survivorship

Address pulmonary rehabilitation, psychosocial support, chronic respiratory or cardiovascular sequelae, and ongoing care for progressive impairment.

Establish models of care

Community-based, integrated, and home-based models responsive to patient needs

Secure sustained funding

Dedicated budget lines; NTP-palliative care program collaboration

Palliative care relieves suffering, improves **quality of life** *, and has been shown to improve* **TB treatment adherence** *and outcomes*

Thank you for your attention

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0 Instructions – DR-TB treatment and care

Regional TB Workshop, Addis Ababa, 23 to 25 June 2026 | One card per group, per group-work slot

Choose the topics that are most applicable to your country context, related to WHO guidance on programmatic management of drug-resistant TB (focused on DR-TB treatment and care), for example:

- Political commitment (available budget, national policy updates, functional working group)
- Advocacy and community engagement (coordination mechanism, awareness campaigns, collaboration with affected communities, involvement of civil society/survivors in planning/technical forums)
- PSM aspects (forecasting mechanism, procurement, paediatric formulations, AE management drugs)
- Capacity building (updated materials, training plan, trained staff, training conducted, safety monitoring tools)
- National guidelines (decentralized treatment initiation, support from expert committee/consilium, investigations for monitoring, treatment adherence support, management of comorbidities, community involvement)
- aDSM (advanced aDSM package, drug safety monitoring board, guidance on AE management, reporting on safety)
- Quality data (AE reports, treatment outcomes, data use)
- Person-centred approach (educational materials, stigma reduction, free services, palliative care, social protection)

1 Group Capture Card

Regional TB Workshop, Addis Ababa, 23 to 25 June 2026 | One card per group, per group-work slot

Session / theme
DR-TB treatment and care

Time slot
Day 1, 14:00 to 14:30

Tool(s) used
Not applicable (brainstorm session)

Rapporteur
[name, country]

Countries in the group
[2 to 4 countries, use the same grouping as for planning groupwork]

Partners present
[list partners]

Fill during the group-work slot. Present this card in the feedback slot.

2 Findings: lessons from implementation

What the group learned about programmatic implementation

Key achievements (up to 3)

- *[achievement 1]*
- *[achievement 2]*
- *[achievement 3]*

Key bottlenecks OR programmatic gaps

- *[bottlenecks/gaps 1]*
- *[bottlenecks/gaps 2]*
- *[bottlenecks/gaps 3]*

Best practices and enablers

- *[Enabler or good practice 1]*
- *[Enabler or good practice 2]*
- *[Enabler or good practice 3]*