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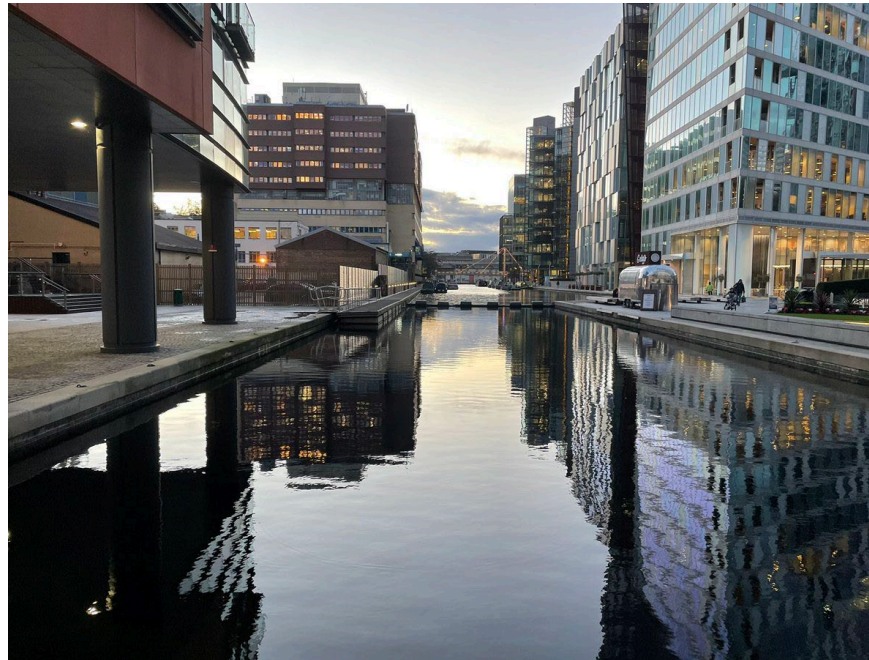
UK Health
Security
Agency

IMPERIAL

MDR TB Webinar

British Thoracic Society

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NHS Trust

Definitions WHO 2025

- **Drug-resistant TB (DR-TB):** TB disease caused by a strain of *Mycobacterium tuberculosis* complex that is resistant to any TB medicines.
- **Drug-susceptible TB (DS-TB):** A bacteriologically confirmed or clinically diagnosed case of TB without evidence of infection with strains resistant to rifampicin and isoniazid.
- **Rifampicin-resistant TB (RR-TB):** TB disease caused by a strain of *M. tuberculosis* complex that is resistant to rifampicin. These strains may be susceptible or resistant to isoniazid (i.e. multidrug-resistant TB [MDR-TB]), or resistant to other first-line or second-line TB medicines.
- **Multidrug-resistant TB (MDR-TB):** TB disease caused by a strain of *M. tuberculosis* complex that is ***resistant to rifampicin and isoniazid***.
- **Pre-extensively drug-resistant TB (pre-XDR-TB):** TB disease caused by a strain of *M. tuberculosis* complex that is ***resistant to rifampicin (and may also be resistant to isoniazid), and that is also resistant to at least one fluoroquinolone*** (either levofloxacin or moxifloxacin).
- **Extensively drug-resistant TB (XDR-TB):** TB disease caused by a strain of *M. tuberculosis* complex that is ***resistant to rifampicin (and may also be resistant to isoniazid), and that is also resistant to at least one fluoroquinolone (levofloxacin or moxifloxacin) and to at least one other “Group A” drug (bedaquiline or linezolid)***.

Abbreviations

- B - bedaquiline
- C - clofazimine
- Cs - cycloserine
- D - delamanid
- E - ethambutol
- Eto - etionamide
- H - isoniazid
- Hh - isoniazid high dose
- L - linezolid
- Lfx - levofloxacin
- M - moxifloxacin
- Pa - pretomanid
- P - rifapentine
- R - rifampicin
- Z - pyrazinamide

New MDR regimens

Trial	Regimen	Duration (weeks)	Trial	Regimen	Duration (weeks)
ZeNix	BPaL with different linezolid dosing schedules	26 weeks	TB- PRACTECAL	BPaLM	24 weeks
		(extend treatment to 39 weeks if ongoing active disease was suspected between weeks 16 and 26)		BPaL BPaLC	
STREAM (stage 2)	9 month all-oral regimen Intensive phase: 16 weeks (extended up to 24 weeks for delayed smear conversion) B(6)+Lfx/M+Eto+C+E + Z+Hh Continuation phase: 24 weeks LfxCEZB	40 weeks	BEAT-TB	BDLLfxC	24 weeks
		28 weeks	endTB	BLMZ BCLLfxZ BDLLfxZ DCMZ DCLLfxZ	39 weeks
	6-month regimen Intensive phase 8 weeks LfxCZBKHh Continuation phase: 20 weeks LfxCZB				

WHO summary recommendations on drug-resistant TB treatment*

1. Treatment of drug-resistant TB using 6-month regimens

1.1 The 6-month bedaquiline, pretomanid, linezolid and moxifloxacin (**BPaLM**) regimen

for MDR/RR-TB and pre-XDR-TB WHO suggests BPaLM rather than 9-month or longer (18-month) regimens in MDR/RR-TB patients (Conditional recommendation, very low certainty of evidence)

1.2 The 6-month bedaquiline, delamanid, linezolid, levofloxacin and clofazimine (**BDLLfxC**) regimen (**BEAT TB**)

WHO suggests the use of a 6-month treatment regimen BDLLfxC in MDR/RR-TB patients with or without fluoroquinolone resistance. (Conditional recommendation, very low certainty of evidence)

Health warning – just updated Sept 2026



WHO summary recommendations on drug-resistant TB treatment ii

2. Treatment of drug-resistant TB using 9-month regimens

2.1 The 9-month all-oral regimen for MDR/RR-TB

WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. (Conditional recommendation, very low certainty of evidence)

2.2 The modified 9-month all-oral regimens for MDR/RR-TB (END TB regimes)

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

- BLMZ > BLLfxCZ > BDLLfxZ

(Conditional recommendation, very low certainty of evidence)

2.3 WHO suggests **against** using 9-month DCLLfxZ or 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 longer regimens WHO 2025

3.1 All three Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of the treatment if bedaquiline is stopped.

If only one or two Group A agents are used, both Group B agents are to be included.

If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it.

(Conditional recommendation, very low certainty of evidence)

Table 3.1. Grouping of medicines recommended for use in longer MDR-TB regimens^a

Groups and steps	Medicine	Abbreviation
Group A: Include all three medicines	Levofloxacin <i>or</i> moxifloxacin	Lfx Mfx
	Bedaquiline ^{b,c}	Bdq
	Linezolid ^d	Lzd
Group B: Add one or both medicines	Clofazimine	Cfz
	Cycloserine <i>or</i> terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E
	Delamanid ^e	Dlm
	Pyrazinamide ^f	Z
	Imipenem–cilastatin <i>or</i> meropenem ^g	Ipm–Cln Mpm
	Amikacin (<i>or</i> streptomycin) ^h	Am (S)
	Ethionamide <i>or</i> prothionamide ⁱ	Eto Pto
	<i>P</i> -aminosalicylic acid ^j	PAS



Implementing shorter all-oral treatment durations for multidrug-resistant tuberculosis in the UK: from concept to application

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doi:10.1136/bmjresp-2025-003861

Table 2 UK approach to support regimen selection

Regimen	Duration	Drug regimen	Pre-XDR TB (Fq resistance)	XDR-TB	Extensive pulmonary disease	Extra-pulmonary TB	HIV	Pregnancy/breastfeeding	Age<14 years
BPaLM/BPaL	6 months (Extend to 9 months if C+ at months 4–6, or clinical judgement)	BPaLM	Yes: use BPaL	No	Yes	Yes—except TB involving CNS, miliary TB and osteoarticular or disseminated TB	Yes	No	No
BEAT-TB	6 months	BDLLfxC (In trial, they continue regimen with fq regardless of fq susceptibility status)	Yes	No	Yes	Excluded complicated or severe extrapulmonary manifestations of TB, including osteoarticular, pericardial and central nervous system infections	Yes	Yes	Yes
endTB	9 months	BLMZ>BLLfxCZ>BDLLfxZ	No	No	Yes	No	Yes	Not studied but drugs used in regimen in pregnancy and breastfeeding	No
9-month all-oral regimen	9 months	Ethionamide variation: Initial phase: 4–6 B(6m)-Eto-Lfx/M-C-Z-E-Hh Continuation phase: 5 Lfx/M-C-Z-E Linezolid variation: Initial phase: 4–6 B(6m)-L (2m)-Lfx/M-C-Z-E-Hh Continuation phase: 5 Lfx/M-C-Z-E If sputum remains positive at month 4, the initial phase is extended to 6 months. B can be extended from 6 to 9 months if the initial phase is prolonged from 4 to 6 months.	No	No	No	Yes—except TB meningitis, miliary TB, osteoarticular TB and pericardial TB	Yes	Use linezolid variation regimen in pregnancy	Yes
Longer individualised 18 months	>18 months	Treatment starts with at least four TB agents likely to be effective At least three agents are included for the rest of the treatment if bedaquiline is stopped If only one or two group A agents are used, both group B agents are to be included If the regimen cannot be composed with agents from groups A and B alone, group C agents are added to complete it.	Yes	Yes	Yes	Yes—some consideration for CNS active drugs	Yes	Yes	Yes

Key points: Drug susceptibility testing (DST) to fluoroquinolones is strongly encouraged, but DST should not delay treatment initiation with regimens that are also effective in patients with pre-XDR-TB. All regimens for MDR/RR-TB require patients to have <1 month prior exposure to drugs in the regimen. Decisions on appropriate regimens should be made according to clinical judgement and patient preference, DST results, treatment history, risk of adverse events and severity and site of the disease. Additional factors if several regimens are possible – • Drug intolerance, • Adverse effect profile • Pill burden • Treatment history, previous exposure to regimen or component drugs • Patient preference. All treatment should be delivered under WHO-recommended standards, including patient centred care and support, informed consent where necessary; principles of good clinical practice, active drug safety monitoring and management, and regular monitoring of patients and drug resistance to assess regimen effectiveness.

B, bedaquiline; BDLLfxC, bedaquiline, delamanid, linezolid, levofloxacin and clofazimine; BDLLfxZ, bedaquiline, delamanid, linezolid, levofloxacin and pyrazinamide; BLLfxCZ, bedaquiline, linezolid, levofloxacin, clofazimine and pyrazinamide; BLMZ, bedaquiline, linezolid, moxifloxacin and pyrazinamide; BPaL, bedaquiline, pretomanid and linezolid; BPaLM, bedaquiline, pretomanid, linezolid and moxifloxacin; C, clofazimine; CNS, central nervous system; D, delamanid; E, ethambutol; Eto, ethionamide; fq, fluoroquinolone; Hh, high dose isoniazid; L, linezolid; Lfx, levofloxacin; M, moxifloxacin; Pa, pretomanid; TB, tuberculosis; XDR-TB, extensively drug-resistant tuberculosis; Z, pyrazinamide.

Chavda A, et al. BMJ Open Respiratory Research. 2026 Apr 2;13(1):e003861.
doi:10.1136/bmjresp-2025-003861

PRE XDR TB – ?WHAT REGIMES

Bedaquiline, delamanid, linezolid, and clofazimine for rifampicin-resistant and fluoroquinolone-resistant tuberculosis (endTB-Q): an open-label, multicentre, stratified, non-inferiority, randomised, controlled, phase 3 trial



- endTB-Q trial
- BDLC 6/9 months
- findings support the use of BDLC, alongside other recommended regimens, for people with pre-XDR tuberculosis who have limited disease at baseline
- For those with pre-XDR tuberculosis and extensive disease, a longer or reinforced regimen might be necessary to prevent unfavourable outcomes

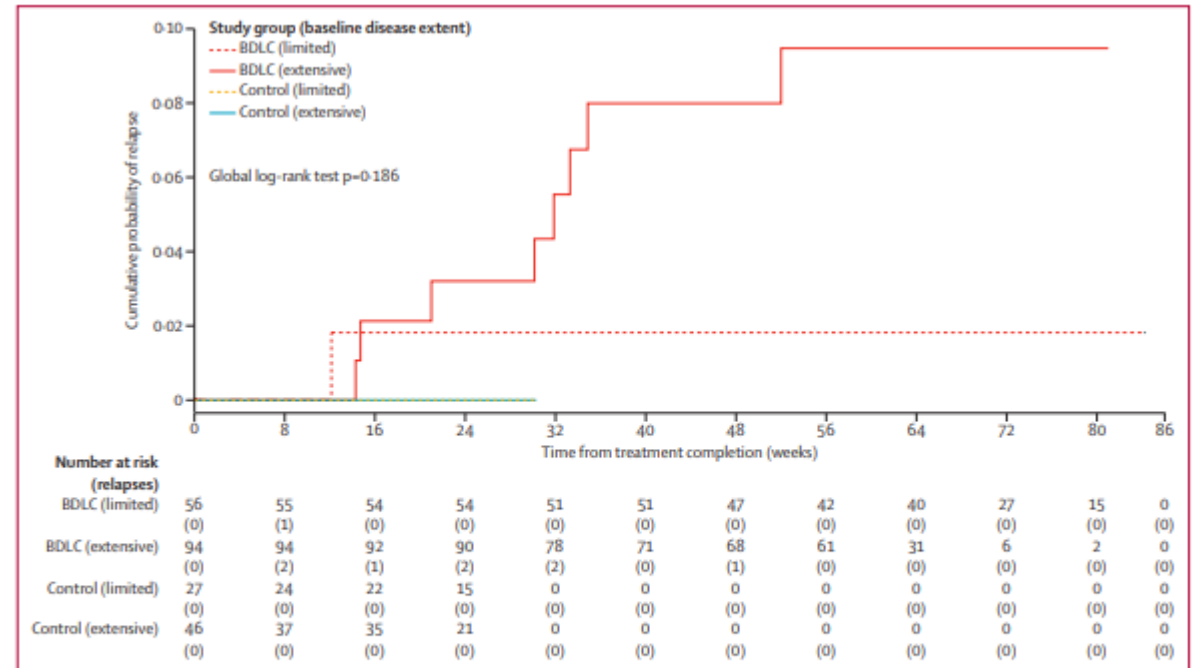


Figure 3: Kaplan-Meier plot of time to relapse (from treatment completion) by baseline extent of tuberculosis disease in the mITT population. Observations censored at the time of post-treatment end of follow-up (early study discontinuation, death, or end of follow-up). Baseline disease extent (limited disease was defined by a negative or scanty smear for *M. tuberculosis* irrespective of cavitation or smear 1+ in the absence of cavitation and extensive disease was defined by smear 2+ or 3+ irrespective of cavitation or smear 1+ in the presence of cavitation). BDLC=bedaquiline, delamanid, linezolid, and clofazimine. mITT=modified intention-to-treat.

WHO REVISION SEPT 2026: B1. TREATMENT OF DRUG-RESISTANT TB USING 6-MONTH REGIMENS

B1.1

WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid and moxifloxacin (BPaLM) rather than the 9-month or longer (18-month) regimens in MDR/RR-TB patients (UPDATED). (Conditional recommendation, very low certainty of evidence)

B1.1a WHO suggests the use of a 6-month regimen composed of bedaquiline, pretomanid and linezolid (BPaL) in patients with non-severe pulmonary pre-XDR-TB (see remarks) rather than the BPaLC regimen (NEW).

(Conditional recommendation, very low certainty of evidence)

B1.1b WHO suggests the use of a 6-month regimen composed of bedaquiline, pretomanid, linezolid and clofazimine (BPaLC) in patients with severe pulmonary pre-XDR-TB (see remarks) rather than the BPaL regimen (NEW). (Conditional recommendation, very low certainty of evidence)

WHO REVISION SEPT 2026:
B1.2 THE 6-MONTH BEDAQUILINE, DELAMANID,
LINEZOLID, LEVOFLOXACIN AND CLOFAZIMINE (BDLLFX/C) REGIMEN

B1.2 WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid, levofloxacin and clofazimine (BDLLfx/C) in MDR/RR-TB patients with or without fluoroquinolone resistance (UPDATED). (Conditional recommendation, very low certainty of evidence)

B1.2a WHO suggests the use of a 6-month BDLC regimen in patients with non-severe pulmonary pre-XDR-TB (see remarks) over the currently recommended longer (18 months or longer) regimens (NEW).

(Conditional recommendation, very low certainty of evidence)

B1.2b WHO suggests against using the 6-month BDLC regimen in patients with severe pulmonary pre-XDR-TB (see remarks) compared to the currently recommended longer regimens (18 months or longer) (NEW).

(Conditional recommendation, very low certainty of evidence)

WHO RAPID COMMUNICATION

13 FEB 2024

TB preventive treatment for contacts of MDR-TB

WHO has recommended TPT for contacts of MDR/RR-TB since 2017.

This recommendation was conditional, based on evidence of very low certainty and is not specific to use of any particular drug regimen.

Its implementation has thus been poor.

A regimen of 6 months of levofloxacin should now be used as TPT for contacts of MDR/RR-TB in light of new evidence from two well-conducted randomized controlled trials in South Africa and Viet Nam supporting the use of levofloxacin of this regimen in people of all ages

UKHSA TB Contact Tracing is available online
Tuberculosis (TB) contact tracing guidance - GOV.UK

<https://www.gov.uk/government/publications/tuberculosis-tb-contact-tracing-guidance>

