RRTB / MDRTB Short Regimen 9-11 months Adults ≥12yrs

Inclusion criteria

- Patients ≥12 years (≥30kg) with RR / MDRTB single mutation / Rif Mono
- Uncomplicated disease PTB / EPTB e.g. lymphadenopathy, Pleural effusion
- Pregnant women who meet criteria above – request through NCAC

Exclusion criteria

- Prior exposure to 2nd line anti-TB agents >1 month
- PreXDR / XDR
- MDRTB with dual mutation (both inhA and Kat G mutation)
- MDRTB with resistance to BDQ, CFZ or LZD
- When additional 2nd line drug resistance is suspected
  - E.g. Close contact with XDR / PreXDR / MDR Dual mutation / Second line treatment failure (request extended DST)
- Complicated / Severe EPTB (CNS / osteo-articular / pericardial effusion / Abdominal TB / TBM)
- Extensive lung disease e.g. bilateral severe pulmonary cavitation
- HB <8g/dl or neutrophils <0.75 or platelets <50 (cannot use LZD)
- If uncertain for eligibility for short regimen

4-6 months (Intensive phase)

LZD $_{(2m)}$ + BDQ $_{(6m)}$ + LFX + CFZ + Z + H^h + E

5 Months (continuation phase)

LFX + CFZ + Z + E

- Give LFX for full 6 months. May switch LFX to MOX when BDQ completed if needed.
- Linezolid for 2 months: Dio FBC 2w, 4w and then monthly whilst taking LZD
- *INH not to exceed 10mg/kg.* If Kat G or InhA mutation: continue for full four months.
- If smear negative by end month 4 and good clinical response: stop INH (continuation ph)
- Intensive phase is 4 months and may be extended to 6 months if smear positive at 4m
- BDQ* can be extended to 9 months if extensive disease , or late conversion or 2nd line uninterpretable / not available. For all extensions apply through NCAC
- If PZA or ethambutol not tolerated: can be withdrawn without being replaced.

	2 MONTHS	4 MONTHS	6 MONTHS	9 MONTHS
Linezolid		Give LZD for 2m		
HDINH			Extend for 2m if smear positive at month 4	
Bedaquiline				Can extend to 9m*
Levofloxacin				
Clofazamine				
Pyrazinamide				
Ethambutol				

Key: H^h : Isoniazid / LZD: Linezolid / LFX: Levofloxacin/Eto: Ethionamine /PZA: Pyrazinamide/BDQ: Bedaquiline /E:Ethambutol/ TRD: Terizidone /DLM: Delamanid NCAC: National Clinical Advisory Committee

Province of the EASTERN CAPE HEALTH — Nkqubela TB Hospital

RRTb / MDRTB Long Regimen 18-20months
Adults ≥12 yrs (≥30kg)

Inclusion criteria

- RR / MDRTB with prior exposure to 2nd line anti-TB agents >1 month
- MDRTB with dual mutation (Kat G and inhA mutation)
- PREXDR with INJ resistance but Sensitive to FLQ
- RR / MDRTB who had close contact with MDR Dual mutation
- RR / MDRTB Complicated / Severe EPTB (pericardial or osteoarticular disease / Abdominal TB)
- RR / MDRTB Extensive lung disease e.g. bilateral severe cavitation
- RR / MDRTB If clinician unsure if the patient meets the criteria for short regimen
- Hb<8g/dl or neutrophils <75 or platelets <50 at baseline or while on LZD in first 2 months of short regimen (discuss regimen with NCAC)

Exclusion criteria

- Any patient with FLQ resistance or close contact with FLQ resistance (present to NCAC)
- TB meningitis (see separate regimen)

MDRTB LONG REGIMEN

6-8 months (Intensive phase)

BDQ $_{(6m)}$ +LZD + LFX + CFZ + TRD

12 Months (continuation phase)

LFX + CFZ + TRD

- BDQ can be extended to 9 months if extensive disease, late conversion or if 2nd Line uninterpretable / unavailable or if FLQ sensitivity not confirmed. Apply through NCAC
- The Intensive phase is 6-8 months depending on **culture conversion** and clinical response. Extend to 8 months if slow clinical response / bilateral pulmonary disease with extensive cavitations / delayed culture conversion)
- LFX may be changed to Moxifloxacin when BDQ completed.

Adverse events / Substitutions

Always discuss substitutions with NCAC

- LZD:
  - Do FBC at baseline, 2w, 4w and monthly. If HB <8g/dl / neutr <0.75 / platelets <50: discontinue LZD and replace with two category C drugs
  - Do visual acuity at baseline and monthly
- TRD: If history of psychosis or patient develop psychosis: substitute TRD with two category C drugs.
  - Always ask about peripheral neuropathy
- If toxicity to one of the five core drugs substitute with two Group C drugs : Ethambutol / PZA / Meropenem / Amikacin / Ethionamide (consult NCAC)
- BDQ: do ECG baseline and monthly.

Key: H[h] : Isoniazid / LZD: Linezolid / LFX: Levofloxacin/Eto: Ethionamine /PZA: Pyrazinamide/BDQ: Bedaquiline /E:Ethambutol/ TRD: Terizidone /DLM: Delamanid NCAC: National Clinical Advisory Committee

Province of the EASTERN CAPE HEALTH
Nkqubela TB Hospital

XDRTB or FLQ resistant regimens: Individualised Adults ≥12yrs

Inclusion criteria

- FLQ resistant TB (e.g. PreXDR with FLQ resistance)
- XDRTB
- Treatment failure on RR / MDRTB regimen

Principles

- Treatment regimens should be individualised considering the history and DST result
- Intensive phase with minimum 4 drugs known or predicted to be effective
- Continuation phase minimum 3 drugs known or predicted to be effective
- A history of a drug used for >1month with persistent smears or positive cultures: consider probable resistance to that drug and do not use it as a core drug. This includes a patient who was started on MDRTB regimen but DST results were delayed.
- Drugs exposed to previously > 1year on positive cultures should not be included in regimen

EXAMPLE of Individualised regimen

6-8 months (Intensive phase)

BDQ $_{(6m)}$ +LZD + (PAS or DLM$_{6m}$) + CFZ + TRD +

+ Z + (Eto or H^{h} *)

12 Months (continuation phase)

LZD + CFZ + TZD + Z +(Eto or H^{h})*

- BDQ can be extended to 9 months if extensive disease, late conversion or 2nd Line uninterpretable or unavailable. Apply through NCAC.
- Regimens should be further individualised using DST and LPA results
- The Intensive phase is 6-8 months depending on **culture conversion** and clinical response
- LZD given at 600mg od. LZD can be reduced to 300mg if toxicity occurs. This is a key drug. If not tolerated discuss with NCAC
- PAS at 4g bd or 8g od. PAS has to be taken with acidic food such as amazi / Morvite
- *Use HDINH if inhA mutation detected; Eto if Kat G mutation and neither INH or ETO in dual mutation
- Have a low threshold to stop PZA of adverse events. NO need to replace

Discuss with NCAC when:

- Resistance suspected or detected to core drugs
- Patient has had treatment >1m with LZD, BDQ, DEL or CFZ in the past
- Core drugs contraindicated or patient cannot tolerate core drugs
- Previously treated for XDR / PreXDR for >1month
- Pregnant patients
- Diagnosed of FLQ resistance >1month on short regimen

Key: H^{h} : Isoniazid / LZD: Linezolid / LFX: Levofloxacin/Eto: Ethionamine /PZA: Pyrazinamide/BDQ: Bedaquiline /E:Ethambutol/ TRD: Terizidone /DLM: Delamanid NCAC: National Clinical Advisory Committee

Province of the EASTERN CAPE HEALTH
Nkqubela TB Hospital

CNS Long regimen Individualised Adults ≥12yrs ≥ 30kg

Inclusion criteria

- Patients with confirmed or highly probable TBM

Principles

- High mortality - seek specialist advice,
- Low threshold to investigate (CT or LP). Every effort to be made to send CSF for GeneXPert / culture and DST
- Cover for bacterial meningitis: Ceftriaxone 2g IVI bd 10 days
- Rule out Cryptococcal meningitis with a CSF CrAG
- ART is initiated after 4-6 weeks.
- Use drugs with good CSF Penetration (LFX / LZD / TZD / Z / ETO / HDINH)
- Discuss all children <12 years (<30kg) with an expert

TBM regimen

6-8 months (Intensive phase)

BDQ (6m) + LZD + LVX + CFZ + TRD +
+ Z +(Eto or H^h)*

12 Months (continuation phase)

LFX + CFZ + TRD + Z + (Eto or H^h *) + (LZD)

- IF FLQ resistance discuss with NCAC – may need additional IVI Carbapenem / Delamanid should be added.
- Use high dose LFX (1000mg in adults) and INH at 15mg/kg/day
- The Intensive phase is 6-8 months depending on **culture conversion** and clinical response
- LZD 600mg od: can be reduced to 300mg if toxicity occurs. If well tolerated can be extended into continuation phase
- Consider adding delamanid as good CNS penetration has been demonstrated in rats
- *Use H^h at 15mg/kg/day if inhA/mutation present / Eto if Kat G mutation / neither in dual mutation
- Repeat CTs may be used to monitor tuberculomas. Residual lesions may be present at end of treatment and do not necessarily represent treatment failure

Steroid use for TBM

Dexamethasone 12mg bd IVI (60kg) - (0,4mg/kg/d): initial stabilization period
Followed by: Prednisone 120mg daily po (2mg/kg/day) for 1 week
Taper dose over 6-8weeks

Key: H^h : Isoniazid / LZD: Linezolid / LFX: Levofloxacin/Eto: Ethionamine /PZA: Pyrazinamide/BDQ: Bedaquiline /E:Ethambutol/ TRD: Terizidone /DLM: Delamanid NCAC: National Clinical Advisory Committee

Province of the EASTERN CAPE HEALTH
Nkqubela TB Hospital