CHILD
< 6 yrs

# The Basic Long RRTB Regimen: FLQ Sensitive (18-20m)
# Children <6 yrs OR < 16kg

## WHO CAN BE INITIATED ON THE BASIC LONG REGIMEN

- Rif Resistant TB that is FLQ SENSITIVE
- There is NO SHORT REGIMEN for children < 6 years at present. This may be revised if BDQ dosing becomes available for children < 6 years old

## WHO MAY NOT BE INITIATED ON THE BASIC LONG REGIMEN

- Any patient with FLQ resistance or close contact with FLQ resistance (present to NCAC)
- Patients who need a rescue regimen
- TB meningitis (see separate regimen)

## PRINCIPLES

- All children < 6 years should be treated by an experienced clinician
- Treatment should be based on DST pattern of most likely source patient
- All attempts should be made to source a sputum on the child, ideally through sputum induction.
- Children with non-severe disease can be treated for 9-15 months. Severe disease will require 12 to 18 months.

Key: HH: Isoniazid / LZD: Linezolid / LFX: Levofloxacin/ CFZ: Clofazamine PZA: Pyrazinamide/ BDQ: Bedaquiline /EMB: Ethambutol/ TRD: Terizidone / DLM: Delamanid NCAC: National Clinical Advisory Committee

## CHILDREN 3-5 Years

LFX + LZD+ CFZ + TRD+ (DLM or PAS)

## CHILDREN <3 years

LFX + LZD+CFZ + TRD + (PAS or ETO or HH)

- Delamanid can be used in children over 3 years old & >16kg
- Use at east 4 active drugs in intensive phase with possible addition of a fifth drug in first few months in cases of severe disease. .
- There is no specified intensive or continuation phase for these regimens and all drugs continued throughout duration of treatment, unless limited by toxicity or intolerance.
- Do not routinely use EMB or PZA - of little benefit to majority of children
- High dose INH may be considered but be careful to not add drugs unless they have a role to play (increased toxicity). Use High dose INH only if InhA mutation present and ETO only if Kat G present.

## ADVERSE EVENTS AND SUBSTITUTIONS

*Always discuss substitutions with NCAC.*

- LZD need close monitoring. Monitor HB according to age range. If there is a drop in HB discuss with NCAC
- If any of the drugs have to be discontinued: substitute with other group C medications.

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CHILD
< 6 yrs

# RRTB FLQ resistant Long Regimen
# Children < 6yrs or <16kg

## WHO IS ELIGBLE FOR THE FLQ-RESISTANT LONG REG

- FLQ resistant TB
  - XDRTB
  - PreXDR with FLQ resistance

## WHO MAY NOT BE INITIATED ON THE FLQ-RES LONG REG

- Patients on either longer or shorter regimen who have a positive culture at month 4 – consider a rescue regimen
- Patents who have failed on a previous RRTB regimen (or index case) – especially if it contained BDQ, LZD and /or CFZ
- Patients with suspected resistance (or index case) to BDQ / LZD / CFZ or confirmed resistance to any of those three.

## PRINCIPLES

- Treatment regimens should be individualised considering the history and DST result
- LZD is a powerful drug and if possible should be used throughout treatment – Note that normal HB levels vary by age
- Treatment duration is 18 months but could be extended to 20 months per clinician discretion

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## Children age 3-5 years

LZD + CFZ + TRD +DLM + (PAS OR ETO)

## Children age <3 years: Discuss all patients with an expert

LZD + CFZ + TRD + PAS + (HH OR ETO)"+ consider DLM

- Use at east four active drugs in intensive phase with possible addition of a fifth drug in first few months in cases of severe disease.
- For <3years benefit of Delamanid probably outweigh risks and should be strongly considered
- Use 4 drugs in continuation phase if extensive disease or co-morbid disease.
- There is no specified intensive or continuation phase for these regimens and all drugs continued throughout duration of treatment, unless limited by toxicity or intolerance.

## Discuss with NCAC when:

- Discuss all children < 6 years with NCAC / expert
- Resistance suspected or detected resistance to core drugs
- Patient has had treatment >1m with LZD, BDQ, DLM CFZ
- Core drugs contraindicated or patient cannot tolerate core drugs
- Previously treated for XDR / PreXDR for >1month
- Diagnosed of FLQ resistance >1month on short regimen
- Send eDST if resistance to LZD, BDQ, CFZ or DLM suspected

CHILD
< 6 yrs

# RRTB CNS Long regimen

## Children < 6yrs or <16kg

## WHEN TO USE THE CNS LONG REGIMEN

- Patients with confirmed or highly probable TBM

## <6 years years

LFX+ LZD + TZD + PZA + ( HH Or ETO*) + DLM

## 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
- 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
- Treatment duration is 18 months but could be extended to 20 months per clinician discretion
- Repeat CTs may be used to monitor tuberculomas. Residual lesions may be present at end of treatment and do not necessarily represent treatment failure

## PRINCIPLES

- For <3years benefit of Delamanid probably outweigh risks and should be strongly considered
- *Use HH only if inhA/mutation present.
- Use ETO only if Kat G mutation present. Use neither in dual mutation
- PZA and either HH or ETO is included because of relatively good CNS penetration
- In continuation phase choose between LZD, ETO or HH depending on INH mutation and tolerance.
- All patients on INH or TZD must be on pyridoxine
  - 25mg/ day age 5-12 years;
  - 12,5MG <5 Years.
  - Pyridoxine does not prevent LZD induced PN.

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# DOSING chart Children <30kg Nov 2019

| Drug | Tablet size | *Average daily dose | Weight Class | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 3-3.9kg | 4-4.9kg | 5-6.9kg | 7-9.9kg | 10-15.9kg | 16-23.9 | 24-30kg | >30kg |
| BDQ | 100mg | | | | | | | 200mg 2w then 100mg M/W/F for 22w | | adult |
| LZD | 600mg tab | 10mg - 12/kg >16yrs / 15mg/kg <16 yrs | | 60mg | 90mg | 120mg | 150-180 | 180-210 | 300 | adult |
| LZD | 20mg/ml | 10mg - 12/kg >16yrs / 15mg/kg <16 yrs | | 70mg | 80mg | 120mg | 160-200 | 160-220 | | |
| LVX | 250mg scored | 15-20mg/kg/day | 62,5 | 75 | 125 | 150 | 250-375 | 375-500 | 500 | adult |
| LVX | 100mg disp tab | 15-20mg/kg/day | 60 | 80 | 100 | 150 | 200-300 | 300-400 | 500 | adult |
| CFZ | 100mg gel cap | 2-5mg/kg/day | | | 100mg M/W/F | | | 100mg alt days | 100mg | adult |
| PZA | 500mg | 30-40mg/kg/day | | | 250 | 250 | 500 | 750 | 1000 | adult |
| PZA | 150mg disp tab | 30-40mg/kg/day | | | 150 | 300 | 450 | 750 | | |
| EMB | 400mg | 15-25mg/kg/day | 80 | 80 | 120 | 200 | 280 | 400 | 600 | adult |
| EMB | 100mg disp tab | 15-25mg/kg/day | 80 | 100 | 200 | 300 | 400 | | | |
| HHINH | 100, 300mg | 15-20mg/kg/day | 50 | 50 | 100 | 150 | 200 | 300 | 400-450 | adult |
| INH | 100mg /300mg | 10-15mg/kg/day | 50 | 50 | 75 | 100 | 150 | 200 | 200 | adult |
| TZD | 250mg caps | 15-20mg/day | | | 100-125 | 125-175 | 175-250 | 250-500 | 500 | adult |
| DLM | 50mg tab | 100mg bd | | | | | | 25mgbd | 50mgbd | 50mg bd till 35kg |
| PAS | 4g satched | 200-300mg/kg/d | | | 1.5g | 2g | 2-4g | 4-6g | 6-8g | |
| ETO | 250mg | 15-20mg/kg/day | | | 125 | 125 | 250 | 375 | 500 | adult |
| MOX High | 400mg | 10mg -15mg/kg/day | | | 80mg | 120mg | 200mg | 200-300 | 400 | adult |
| MER | 1g vial (20ml) | 20-40mg/kg IVI q8h | | | 100mg | 200mg | 300mg | 400-450 | 550 | adult |
| AM/Clv | 250/62.5mg per 5ml susp | 30 min before each Meropenem dose | | | 25mg | 37.5mg | 62.5mg | 100mg | 125mg | adult |
| AM Inj | 500mg vial (2ml) | 15-25mg/day | | | 100 | 150 | 200-250 | 300-375 | 500 | adult |

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