Annexure B

Western Cape Government FOR YOU

DRUG-RESISTANT-TB TREATMENT DOSING TABLE FOR CHILDREN 2024

(< 46 kg and < 15 years)

MEDICINES INFORMATION CENTRE

	WHO Group A									WHO Group B			
	Levofloxacin (LFX) (preferred quinolone)		**Moxifloxacin (MFX)**	**Bedaquiline (BDQ)**		**Linezolid (LZD)**				**Terizidone (TRD)#**	**Clofazimine (CFZ)**		
Formulations	100 mg DT** **OR** 10 mg/mL suspension	250 mg tablet **OR** 500 mg tablet **OR** 25 mg/mL suspension	400 mg tablet	20 mg DT	100 mg tab **OR** 10 mg/mL suspension	20 mg/mL suspension	150 mg DT** **OR** 15 mg/mL suspension	600 mg tablet **OR** 60 mg/mL suspension		250 mg capsule	50 mg DT** **OR** 5 mg/ml suspension	100 mg gel capsule	**Formulations**
Target dose	15-20 mg/kg/day		10 - 15 mg/kg/day	Once daily loading dose for 14 days then thrice weekly (TIW) dosing M/W/F		1 - 15 kg: 15 mg/kg per day; ≥ 15 kg: 10-12 mg/kg daily				7 - 29.9 kg: 15 - 20 mg/kg; ≥ 30 kg: 10 - 15 mg/kg	2 - 5 mg/kg when given daily		**Target dose**
MDD	1.5g		400 - 800 mg	Loading dose: 400 mg daily; Maintenance dose: 200 mg M/W/F		600 mg				750 mg	100 mg		**MDD**
Practical advice	In general, for older children able to swallow tablets/capsules whole, avoid crushing and mixing tablets/capsules with water, as this may reduce palatability (tastes worse than swallowing tablets whole). Discard any unused portion of a non-commercial solution. Dispersible tablets (DT) can either be dispersed in a liquid or mixed with a soft or semi-soft food such as a spoonful of yoghurt or porridge												**Practical advice**
	For a 10 mg/mL suspension: crush and disperse 1 x 100 mg DT in 10 mL water	For a 25 mg/mL suspension: crush and disperse 1 x 250 mg tablet in 10 mL water	For 40 mg/mL suspension: crush and disperse 1 x 400 mg tablet in 10 mL water	A daily loading dose for 2 weeks, followed by a maintenance dose given three times a week for 22 weeks. If treatment is interrupted see Table on Bedaquiline interruptions on next page for guidance on reloading. For 10 mg/mL suspension: Crush and disperse 1 x 100 mg tablet in 10 mL water. Vigorous stirring/shaking is needed prior to administrating the 100 mg tablet crushed and suspended in water		Once reconstituted, must be used within 21 days	For 15 mg/mL suspension: crush and disperse 1 x 150 mg DT in 10 mL water	For 60 mg/mL suspension: crush and disperse 1 x 600 mg tablet in 10 mL water		For 25 mg/mL suspension: Open capsule and mix contents with 10 mL water	The 50 mg DT is preferred for children < 24 kg. For 5 mg/mL suspension: crush and disperse 1 x 50 mg DT in 10 mL water	Dosing interval changes as weight of child increases. Soften 1 x 100 mg capsule in 10ml of water or yoghurt and administer entire volume¥	
Wt. (kg)	Consult with a clinician experienced with DR-TB prescribing for children weighing < 5 kg. Refer to adult guidelines in children > 46 kg and > 15 years of age												**Wt. (kg)**
				20 mg DT		**100 mg tab OR 10 mg/mL solution**							
				Loading dose daily for 2 weeks	**Maintenance dose M/W/F for 22 weeks**	**Loading dose daily for 2 weeks**	**Maintenance dose M/W/F for 22 weeks**						
3 - 4.9	5 mL **OR** 0.5 x 100 mg DT daily	2 mL daily	1 mL daily	< 3 months: 1.5 x 20 mg DT daily ≥ 3 months: 3 x 20 mg DT daily	< 3 months: 0.5 x 20 mg DT M/W/F ≥ 3 months: 1 x 20 mg DT M/W/F	< 3 months: 3 mL daily ≥ 3 months: 6 mL daily	< 3 months: 1 mL M/W/F ≥ 3 months: 2 mL M/W/F	2 mL daily	2.5 mL daily		1 mL daily	2-4 mL daily		**3 - 4.9**
5 - 6.9	1 x 100 mg DT daily	5 mL **OR** 0.5 x 250 mg tab daily	2 mL daily					4 mL daily	5 mL **OR** 0.5 x 150 mg DT daily	1.25 mL daily	2 mL daily	5 mL daily	1 x 100 mg cap M/F	**5 - 6.9**
7 - 9.9	1.5 x 100 mg DT daily		3 mL daily	< 3 months: 1.5 x 20 mg DT daily 3 to < 6 months: 3 x 20 mg DT daily ≥ 6 months: 4 x 20 mg DT daily	< 3 months: 0.5 x 20 mg DT M/W/F 3 to < 6 months: 1 x 20 mg DT M/W/F ≥ 6 months: 2 x 20 mg DT M/W/F	< 3 months: 3 mL daily 3 to < 6 months: 6 mL daily ≥ 6 months: 8 mL daily	< 3 months: 1 mL M/W/F 3 to < 6 months: 2 mL M/W/F ≥ 6 months: 4 mL M/W/F	6 mL daily	1 x 150 mg DT daily	2.5 mL daily	5 mL daily		1 x 100 mg cap M/F	**7 - 9.9**
10 - 15.9	2 x 100 mg DT daily	1 x 250 mg tab daily	5 mL daily **OR** 0.5 x 400 mg tab	3 - < 6 months: 3 x 20 mg DT daily ≥ 6 months: 6 x 20 mg DT daily	3 - < 6 months: 1 x 20 mg DT M/W/F ≥ 6 months: 3 x 20 mg DT M/W/F	3 - < 6 months: 6 mL daily ≥ 6 months: 12 mL daily[Δ]	3 - < 6 months: 2 mL M/W/F ≥ 6 months: 6 mL M/W/F	8 mL daily			1 x 250 mg cap daily	1 x 50 mg DT daily	1 x 100 mg cap M/W/F	**10 - 15.9**
16 - 23.9	3 x 100 mg DT daily	1.5 x 250 mg tab daily	7.5 mL daily	10 x 20 mg DT daily	5 x 20 mg DT M/W/F	2 x 100 mg tabs daily	1 x 100 mg tab M/W/F	11 mL daily	2 x 150 mg DT daily[##]	5 mL daily **OR** 0.5 x 600 mg tab daily	2 x 250 mg caps daily	2 x 50 mg DT daily	1 x 100 mg cap daily	**16 - 23.9**
24 - 29.9	5 x 100 mg DT daily	2 x 250 mg tab daily **OR** 1 x 500 mg tab daily	1 x 400 mg tab daily					14 mL daily						**24 - 29.9**
30 - 35.9		1.5 x 500 mg tab **OR** 3 x 250 mg tabs daily		20 x 20 mg DT daily	10 x 20 mg DT M/W/F	4 x 100 mg tabs daily	2 x 100 mg tabs M/W/F	15 mL daily						**30 - 35.9**
36 - 45.9								20 mL daily	3 x 150 mg DT daily	7.5 mL daily				**36 - 45.9**

**Only available via Section 21. Not available at all facilities; ¥If there are any administration difficulties, consult with a TB hospital; [Δ]Use 2 x 100 mg tabs in 20 mL water, and give 12 mL. Discard the rest; #hdINH and TZD: Only to be co-used after consultation with an expert; Add pyridoxine when INH or TZD is prescribed—see dosing under hdINH; ##For weight band 16 - 23.9 kg: Clinicians may opt to administer 1.5 x 150 mg DT or 4 mL of the 60 mg/mL solution to ensure the dose does not exceed 10 - 12 mg/kg; cap = capsule; DT = dispersible tablet; M/W/F = administer medicines three times a week on a Monday, Wednesday and Friday; tab = tablet; MDD = maximum daily dose; TIW = three times a week

	WHO Group C						Other medicines		
	Delamanid (Dlm)		Ethionamide (Eto)	Para-aminosalicylic acid (PAS)[##]	Meropenem[†] + Amoxicillin/clavulanate		High-dose isoniazid (hdINH)[#]		
Formulations	25 mg DT[**]	50 mg tablet **OR** 5 mg/mL suspension	250 mg tablet **OR** 25 mg/mL suspension	4 g sachet	500 mg per vial (10 mL) 1 g powder per vial (20 mL)	250 mg / 62,5 mg in 5 mL suspension 250/125 mg tablet	100 mg tablet **OR** 10 mg/mL suspension	300 mg tablet	Formulations
Target dose	3 - 4 mg/kg/day		15 - 20 mg/kg/day	200 - 300 mg/kg/d	20 - 40 mg/kg IV every 8h	To be used with meropenem	15 - 20 mg/kg/day		Target dose
MDD	100 mg twice daily		1 g	8 g	2 g twice daily	250/125 mg three times a day	600 mg		MDD
Practical advice	Discard any unused portion of a non-commercial solution. Dispersible tablets (DT) can either be dispersed in a liquid or mixed with a spoonful of soft or semi-soft food such as yoghurt or porridge.								Practical advice
	< 3 months: daily dosing ≥ 3 months: twice daily dosing	< 3 months: daily dosing ≥ 3 months: twice daily dosing; For 5 mg/mL suspension: disperse 1 x 50 mg in 10 mL water	For a 25 mg/mL suspension: Crush and disperse 1 x 250 mg tablet in 10 mL water	Ensure patient receives the special measuring spoon to measure the dose correctly. Administer with a spoonful of yoghurt or other soft food with low pH (e.g. apple puree, tomato or orange juice, mague or fermented potato)	Intravenous administration (only to be used with clavulanic acid)	To be given with each dose of the carbapenem. Oral administration, 30 min before IV meropenem. Dosing expressed as clavulanate. Once reconstituted, must be used within 7 days (confirm with specific product information)	For 10 mg/mL suspension: crush and disperse 1 x 100 mg tablet in 10 mL water Pyridoxine (vitamin b6) 1-2 mg/kg/day is always given with high dose INH: < 6 kg: 6.25 mg/d (¼ x 25mg tablet); ≥ 6kg but < 5 years: 12.5 mg/d; ≥ 5 year: 25 mg/d		
Wt. (kg)	Consult with a clinician experienced with DR-TB prescribing for children weighing < 5 kg. Refer to adult guidelines in children > 46 kg and > 15 years of age								Wt. (kg)
3 - 4.9	1 x 25 mg DT daily	5 mL **OR** 0.5 x 50 mg tab daily	Consult with experienced clinician	300 mg (or 0.3 g) twice daily	50 mg (1 mL) IV three times a day	18,75 mg (1.5 mL) three times a day	5 mL daily **OR** 0.5 x 100 mg tab daily		3 - 4.9
5 - 6.9	< 3 months: 1 x 25 mg DT daily; ≥ 3 months: 1 x 25 mg DT twice daily	< 3 months: 5 mL **OR** 0.5 x 50 mg tab daily; ≥ 3 months: 5 mL **OR** 0.5 x 50 mg tab twice daily	3 mL daily	750 mg (or 0.75 g) twice daily	100 mg (2 mL) IV three times a day	25 mg (2 mL) three times a day	1 x 100 mg tab daily		5 - 6.9
7 - 9.9			5 mL daily **OR** 0.5 x 250 mg tab daily	1000 mg (or 1 g) twice daily	200 mg (4 mL) IV three times a day	37.5 mg (3 mL) three times a day	1.5 x 100 mg tabs daily		7 - 9.9
10 - 15.9	1 x 25 mg DT twice daily	5 mL **OR** 0.5 x 50 mg tab twice daily	1 x 250 mg tab **OR** 10 mL daily	2000 mg (or 2 g) twice daily	300 mg (6 mL) IV three times a day	62.5 mg (5mL) three times a day	2 x 100 mg tabs daily		10 - 15.9
16 - 23.9	2 x 25 mg DT in the morning and 1 x 25 mg DT at night	10 mL (1 x 50 mg tab) in the morning and 5 mL (0.5 x 50 mg tab) at night	2 x 250 mg tabs daily	3000 mg (or 3 g) twice daily	450 mg (9 mL) IV three times a day	100 mg (8 mL) three times a day	3 x 100 mg tabs daily	1 x 300 mg tab daily	16 - 23.9
24 - 29.9				3500 mg (or 3.5 g) twice daily	550 mg (11 mL) IV three times a day	250/125 mg tab three times a day[Φ]	4 x 100 mg tabs daily	1.5 x 300 mg tabs daily	24 - 29.9
30 - 35.9	2 x 25 mg DT twice daily	1 x 50 mg tab twice daily		4000 mg (or 4 g) twice daily	1 g (1 vial) three times a day IV **OR** 2 g (2 vials) twice a day IV	250/125 mg tab three times a day or twice a day according to meropenem dosing[Φ]			30 - 35.9
36 - 45.9							4.5 x 100 mg tabs daily		36 - 45.9

[##]If sodium amino salicylate 1g tablets (Monopas®), accessed via section 21, is used, consult expert on administration; [†]In consultation with an experienced clinician, other carbapenems can be considered; [Φ]Alternatively, use 10mL of the 250/62.5 mg/mL syrup two to three times day according to meropenem dosing; [#]hdINH and TZD: Only to be co-used after consultation with an expert; Add pyridoxine when INH or TZD is prescribed; MDD = maximum daily dose

MONITORING FOR ADVERSE REACTIONS TO DR-TB MEDICINES IN CHILDREN

TEST	FREQUENCY	COMMENT
FBC, neutrophil count and platelets	Baseline, at week 2, 4, 6 and 8, and then monthly	Hb < 8, neutrophils < $0.75x10^9$/L or platelets < $50x10^9$/L needs urgent intervention. Often caused by LZD. FBC abnormalities needs urgent attention. Discuss with a specialist
ECG	Baseline, at two weeks, at one month, and then monthly	QTcF > 450msec needs intervention. Also repeat ECG after 2 weeks if >60msec difference from previous QTcF result. If still raised consult with specialist. Fridericia's formula: QTcF: QT/RR(0.33)
Peripheral neuropathy (PN)	Baseline, then monthly	Can be caused by LZD, hdINH and TZD and may be permanent. LZD induced neuropathy occurs mostly with long-term use and does not respond to pyridoxine. Consult with TB specialist
Visual acuity/optic neuritis	Baseline, then monthly	Possible culprits: Ethambutol, LZD, rifabutin
ALT	Baseline, repeat if symptomatic for liver dysfunction	Symptoms of liver toxicity include: nausea and vomiting, right upper quadrant pain and tender liver, visible jaundice. Stop all medicines if ALT > 5 x ULN or if ALT > 3 x ULN with symptoms of liver dysfunction and discuss with an expert
K+ and Mg2+	Baseline, repeat if QTcF is prolonged or vomiting/diarrhoea/clinically unwell	
TSH (if using PAS and/or ethionamide)	Baseline and every 2 - 3 months	If TSH is increased, do free T4. Discuss deranged thyroid functions with a specialist

BEDAQUILINE INTERRUPTIONS

RELOAD AS BELOW AND CONTINUE NORMAL MAINTENANCE DOSE

Duration of interruption	Instructions for reloading
< 2 weeks	No reloading needed
2 - 4 weeks	3 days 400 mg[†] bedaquiline daily
1 - 12 months	7 days 400 mg[†] bedaquiline daily
> 12 months	14 days 400 mg[†] bedaquiline daily

[†]If the patient weighs between 16 and 30 kg, reload with 200 mg daily. If patient < 16kg, consult with an expert

NEED HELP?

Contact the TOLL-FREE National HIV & TB Health Care Worker Hotline

0800 212 506 /021 4066782

Alternatively "WhatsApp" or send an SMS or "Please Call Me" to 071 840 1572

www.mic.uct.ac.za

Western Cape Government FOR YOU | National HIV & TB Health Care Worker Hotline 0800 212 506 | University of Cape Town | MIC Medicines Information Centre | Stellenbosch University iYunivesithi Universiteit

Largely based on the 2023 NDoH Clinical Management of Rifampicin-Resistant Tuberculosis—Updated Clinical Reference Guide.
Additional references available on request

ALT = alanine transaminase; ECG = electrocardiogram; FBC = full blood count; K^+ = potassium; Mg^{2+} = magnesium; QTcF = corrected QT interval using the Fridericia formula

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