South African Drug Sensitive TB Treatment Guidelines - Children

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DIAGNOSIS OF PULMONARY TUBERCULOSIS (PTB) IN CHILDREN

Diagnosis of TB in children is based on a combination of clinical presentation, history of exposure, bacteriology, chest x-ray and tuberculin skin test (Mantoux®)

Clinical (The presence of at least three of these features is suggestive of TB)	• ≥ 2 week history of cough or wheeze • Persistent fever • Weight loss • Unusual fatigue • Physical signs suggestive of TB e.g. enlarged lymph glands and night sweats • Chest x-ray suggestive of TB
Bacteriological	• Positive GeneXpert, smear microscopy, culture and drug sensitivity testing or line probe assay (LPA)

TB TREATMENT IN CHILDREN

Uncomplicated TB in children < 8 years (and/or < 25 kg)	Includes peripheral lymphadenitis; uncomplicated intrathoracic TB (hilar or mediastinal lymphadenopathy, minimal bronchopneumonia, simple pleural effusion)	Refer to **Table A**
Complicated TB (excluding central nervous TB or miliary TB) in children < 8 years (and/or < 25 kg)	Includes complicated/severe intrathoracic TB (extensive bronchopneumonia, cavitatory disease, smear-positive disease, TB empyema); severe forms of extrapulmonary TB (including TB pericarditis, TB abdomen, osteoarticular TB); TB with HIV co-infection	Refer to **Table B**
Miliary TB or TB meningitis/central nervous system TB in children < 8 years (and/or < 25 kg)	Serious forms of TB with brain/meningeal involvement	Refer to **Table C/D**
Uncomplicated and complicated TB in children ≥ 8 years and ≥ 25 kg		Refer to **Table E**

Note: Patients should be weighed regularly and the dose adjusted according to their current weight

TABLE A

UNCOMPLICATED TB DISEASE

CHILDREN < 8 YEARS (OR < 25 KG)

Treatment phase	Intensive phase - daily for 2 months	Continuation phase – daily for 4 months
Body weight (kg)	RHZ 75/50/150 mg dispersible tablet (scored) OR 75/50/150 mg per 4 mL solution*	RH 75/50 mg dispersible tablet (scored) OR 75/50 mg per 4 mL solution*
2–2.9 kg	½ tablet or 2 mL	½ tablet or 2 mL
3–3.9 kg	¾ tablet or 3 mL	¾ tablet or 3 mL
4–7.9 kg	1 tablet or 4 mL	1 tablet or 4 mL
8–11.9 kg	2 tablets or 8 mL	2 tablets or 8 mL
12–15.9 kg	3 tablets or 12 mL	3 tablets or 12 mL
16–24.9 kg	4 tablets or 16 mL	4 tablets or 16 mL

* If oral suspension required, for each dose, disperse **1x RHZ 75/50/150 mg OR 1x RH 75/50 mg** tablet in **4 mL** of water, administer required dose, discard unused suspension

TABLE B

COMPLICATED TB DISEASE (excluding central nervous system TB/miliary TB)

CHILDREN < 8 YEARS (OR < 25 KG)

Treatment phase	Intensive phase - daily for 2 months		Continuation phase – daily for 4—7** months
Body weight (kg)	RHZ 75/50/150 mg dispersible tablet (scored) OR 75/50/150 mg per 4 mL solution*	+ E 400 mg tablet OR 400mg/8mL solution#	RH 75/50 mg dispersible tablet (scored) OR 75/50 mg per 4 mL solution*
2–2.9 kg	½ tablet or 2 mL	1 mL	½ tablet or 2 mL
3–3.9 kg	¾ tablet or 3 mL	1.5 mL	¾ tablet or 3 mL
4–7.9 kg	1 tablet or 4 mL	2.5 mL	1 tablet or 4 mL
8–11.9 kg	2 tablets or 8 mL	½ tablet or 4 mL	2 tablets or 8 mL
12–15.9 kg	3 tablets or 12 mL	¾ tablet or 6 mL	3 tablets or 12 mL
16–24.9 kg	4 tablets or 16 mL	1 tablet or 8 mL	4 tablets or 16 mL

* If oral suspension required, for each dose, disperse **1x RHZ 75/50/150 mg OR 1x RH 75/50 mg** tablet in **4 mL** of water, administer required dose, discard unused suspension

\# If oral suspension required, for each dose, crush **1 x Ethambutol 400 mg tablet** to a fine powder, disperse in **8 mL** of water to prepare a concentration of 400 mg/8 ml (50 mg/ml), administer required dose as indicated in above chart, discard unused suspension

** Guided by expert opinion, the continuation phase may be prolonged to 7 months in slow responders and children with HIV

TABLE C/D

DISSEMINATED (MILIARY) TB OR TB MENINGITIS# IN CHILDREN

Note: The 75/50 RH and 75/50/150 RHZ formulations are not suitable for achieving the required doses in disseminated TB and TBM, so the 60/60 RH formulation should be used.

Body weight (kg)	Single phase of treatment, 6-9 months# Once daily; 7 days a week		
	RH 60/60 mg dispersible tablet (scored) or solution*	+ Z 500 mg tablet (scored) or 500 mg/8 mL suspension**	+ Eto 250 mg tablet (scored) or 250 mg/8 mL suspension***
<2 kg	Obtain Expert Advice		
2-2.9 kg	¾ tablet or 3 mL	1 mL	1.5 mL
3-3.9 kg	1 tablet or 4 mL	2 mL	2 mL
4-4.9 kg	1 ½ tablets or 6 mL	2.5 mL	2.5 mL
5-5.9 kg	1 ¾ tablets or 7 mL	3 mL	3 mL
6-6.9 kg	2 tablets or 8 mL	½ tablet or 4 mL	½ tablet or 4 mL
7-7.9 kg	2 ½ tablets or 10 mL		
9-9.9 kg	3 tablets or 12 mL	¾ tablet or 6 mL	¾ tablet or 6 mL
10-11.9 kg	3 ½ tablets or 14 mL		
12-12.9 kg	4 tablets or 16 mL	1 tablet or 8 mL	1 tablet or 8 mL
13-14.9 kg	4 ½ tablets or 18 mL		
15-16.9 kg	5 tablets or 20 mL		1 ¼ tablet or 10 mL
17-17.9 kg	5 ½ tablets or 22 mL	1 ¼ tablets or 10 mL	
18-19.9 kg			1 ½ tablets or 12 mL
20-24.9 kg	6 tablets or 24 mL	1 ½ tablets or 12 mL	

* If oral solution required, for each dose, disperse **1 x RH 60/60 mg** tablet in **4 mL** of water, administer required dose as indicated in above chart, discard unused solution

If oral suspension is required, crush **1 x 500 mg pyrazinamide tablet to a fine powder, disperse in **8 mL** water to prepare a concentration of 500 mg/8 ml (62.5 mg/ml), administer required dose as indicated in above chart, discard unused suspension

*** If oral suspension is required, crush **1 x 250 mg ethionamide tablet** to a fine powder, disperse in **8 mL** of water to prepare a concentration of 250 mg/8 ml (31.3 mg/ml), administer required dose as indicated in above chart, discard unused suspension

\# For central nervous system TB, consider prolonging treatment for another 3 months if there are concerns about ongoing disease. Discuss with an expert

Note: All cases of miliary TB should have a lumbar puncture (LP) performed. Any abnormal CSF results or where a LP is not performed, should be treated as a patient with TBM

Note: Children should be taught and encouraged to swallow whole tablets or, if required, fractions of tablets so as to avoid large volumes of liquid medication if possible

TABLE E

UNCOMPLICATED AND COMPLICATED TB** IN CHILDREN ≥ 8 YEARS AND ≥ 25 KG

Treatment phase	Intensive phase—daily for 2 months	Continuation phase – daily for 4 months	
Body weight (kg)	RHZE (150,75,400,275)	RH (150,75)	RH (300,150)
25–37.9 kg	2 tablets	2 tablets	
38–54.9 kg	3 tablets	3 tablets	
55–70.9 kg	4 tablets		2 tablets
>71 kg	5 tablets		2 tablets

**Severe forms of TB (central nervous system TB, including TBM, osteoarticular TB (TB of the bones/joints) or miliary TB) in children 25 - 35 kg should be treated with guidance from an expert as higher doses are required. Consult with an expert or the hotline

PYRIDOXINE PROPHYLAXIS

- Children with TB who are HIV-infected, malnourished, or with existing neuropathy: pyridoxine 12.5 mg daily for children < 5 years and pyridoxine 25 mg/day for children > 5 years, for 6 months
- All children with miliary TB: 25 mg daily for 6 months

R = rifampicin, H = isoniazid, Z = pyrazinamide, E = ethambutol, Eto = ethionamide, TBM = TB Meningitis

NEED HELP?

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

0800 212 506 / 021 406 6782

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

www.mic.uct.ac.za

MONITORING RESPONSE TO TREATMENT

Type of monitoring	Frequency of monitoring	Monitoring parameters
Clinical	Monthly for first 2 months, thereafter every 2 months until completion of TB treatment	• Presence of TB symptoms • Treatment adherence—review the patient treatment card, conduct pill count • Adverse events • Weight gain—measure and record the patient's weight • Review medication dosages and adjust according to weight
Bacteriological	At 7 weeks (end of intensive phase) At 23 weeks (end of continuation phase)	• Smear microscopy (where appropriate) • TB culture • If TB culture is positive, do drug susceptibility testing

If poor response to treatment, check for the following: non-adherence to treatment, resistance, other lung diseases etc.

TREATMENT OF TB IN HIV CO-INFECTED CHILDREN

TB develops while on antiretroviral therapy (ART):

ART should be continued throughout TB treatment. TB treatment should be started at standard doses

On efavirenz-based regimen:
- No dosage adjustment required

On dolutegravir-based regimen:
- Rifampicin decreases the concentration of dolutegravir
- Children > 20 kg: give dolutegravir 50 mg in the morning and 50 mg at night. This should be continued for 2 weeks after completion of TB treatment

On lopinavir/ritonavir-based regimen:
- Rifampicin reduces LPV concentration and dosage adjustment required
- Refer to paediatric ARV dosing chart
- LPV/r solution: Super boosting required with additional ritonavir powder twice a day at a dose of 0.75 x the volume of the LPV/r dose
- LPV/r tablets: Double dose LPV/r tablets only in children who can swallow whole tablets (tablets must not be crushed, broken or chewed)

TB diagnosed before starting ART:

Start ART within 2 weeks after starting TB treatment:
- CD4 cell count < 50 cells/µl
- Patients with drug resistant TB at non-neurological site

Start ART within 2-8 weeks after starting TB treatment:
- CD4 cell count ≥ 50 cells/µl

Defer ART 4-8 weeks after starting TB treatment:
- TB meningitis (irrespective of CD4 count)

MANAGEMENT OF COMMON ADVERSE DRUG REACTIONS

Adverse drug reaction	Drug involved	Management
Peripheral neuropathy	Isoniazid	Pyridoxine—for prophylaxis, or treatment once isoniazid toxicity occurs
Hepatitis or jaundice	Rifampicin, isoniazid, pyrazinamide	Stop all drugs. Exclude other causes. Commence at least three antituberculosis drugs with low/no hepatotoxic potential as background therapy. Rechallenge TB treatment in hospital
Gastrointestinal disturbances	Rifampicin, isoniazid, pyrazinamide, ethambutol	Symptomatic treatment
Skin rash	Rifampicin, isoniazid, pyrazinamide, ethionamide	**Mild:** Symptomatic treatment **Severe (skin rash with blistering, mucosal involvement, systemic symptoms):** stop all drugs Once resolved, rechallenge TB drugs in hospital
Loss of colour vision	Ethambutol	Stop ethambutol and refer to eye specialist same day
Joint pain	Pyrazinamide	Give paracetamol 15 mg/kg (up to 1 g) 6 hourly as needed up to 5 days

Based on the National Guidelines for the Management of Tuberculosis in Children 2013, Department of Health, South Africa, and updated dosing based on NDoH circular

Reference: 2021/06/24/EDP/01 and Western Cape H149/2021

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