



health

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NOTICE: AVAILABILITY OF PAEDIATRIC FIXED-DOSE FORMULATIONS FOR MANAGEMENT OF DRUG-SENSITIVE TUBERCULOSIS

The dispersible fixed-dose formulations for the treatment of tuberculosis in paediatrics will be available in the public sector by July 2021.

The National Essential Medicines List Committee have approved the following updated weight-band dosing tables for the management of paediatric:

- A. Uncomplicated pulmonary tuberculosis
- B. Complicated pulmonary tuberculosis
- C. Disseminated (Miliary) TB
- D. Tuberculous meningitis (TBM)

This updated guidance will be included in the Primary Health Care and Paediatric Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) - *See Appendix I.*

Provinces and Health Care Facilities are requested to distribute and communicate this information in consultation with their Pharmaceutical and Therapeutics Committees.

Queries may be submitted to:

Clinical queries

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Kind regards

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Date: 27 June 2021

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Date: 28 June 2021

Updated guidance¹ for the management of paediatric:

- A. Uncomplicated pulmonary tuberculosis
- B. Complicated pulmonary tuberculosis
- C. Disseminated (miliary) tuberculosis
- D. Tuberculous meningitis (TBM)

(This is an update of the Primary Healthcare STGs and EML 2020 edition, Section 17.4: Pulmonary tuberculosis and the Paediatric Hospital Level STGs and EML, 2017 edition, Chapter 10: Tuberculosis)

A: UNCOMPLICATED PULMONARY TUBERCULOSIS				
Indications:				
Includes smear negative pulmonary TB with no more than mild to moderate lymph node enlargement and/or lung field opacification, or simple pleural effusion..				
Dosing:				
» Adjust treatment dosages to current body weight.				
» If calculating dosages, rather give ½ tablet more than ½ tablet less.				
CHILDREN < 8 YEARS OF AGE (OR < 25 kg):				
Note: The patient should be weighed regularly and the dose adjusted according to their current weight.				
Body weight kg	2 months intensive phase given daily		4 months continuation phase given daily	
	RHZ		RH	
	75/50/150 mg dispersible tablet (scored) OR 75/50/150 mg per 4 mL solution*		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	
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 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.				
AND				
<ul style="list-style-type: none"> • Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy: <ul style="list-style-type: none"> ○ Child < 5 years old: 12.5 mg. ○ Child ≥ 5 years old: 25 mg. 				
CHILDREN ≥ 8 YEARS AND ADOLESCENTS (AND ≥ 25 kg):				
Note: The patient should be weighed regularly and the dose adjusted according to their current weight.				
Body weight kg	2 months intensive phase given daily		4 months continuation phase given daily	
	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
AND				
<ul style="list-style-type: none"> • Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy: <ul style="list-style-type: none"> ○ Child < 5 years old: 12.5 mg. ○ Child ≥ 5 years old: 25mg. 				

R=rifampicin, H=isoniazid, Z=pyrazinamide, E=ethambutol

¹ Aligned with: Guidance for national tuberculosis programmes on the management of tuberculosis in children: second edition. Geneva, World Health Organization, 2014. https://apps.who.int/iris/bitstream/handle/10665/112360/9789241548748_eng.pdf?sequen

B: COMPLICATED PULMONARY TUBERCULOSIS

Indications:

- » Includes all other forms of pulmonary TB, such as smear positive TB, cavitary pulmonary TB, bronchopneumonic TB, severe or extensive pulmonary TB lesions, tuberculous empyema.
- » Includes all HIV/TB co-infected cases.
- » Exclude TB meningitis in all cases of miliary TB, refer if this cannot be safely done at current level of care.

Dosing:

- » Weigh at each visit and adjust treatment doses to body weight. If calculating dosages, rather give ½ tablet more than ½ tablet less.
- » Keep strictly to the correct dose and the duration of treatment.

CHILDREN < 8 YEARS OF AGE (OR <25 kg):

Note: The patient should be weighed regularly and the dose adjusted according to their current weight.

Body weight kg	2 months intensive phase given daily		4–7*** months continuation phase given daily
	RHZ	E	RH
	75/50/150 mg dispersible tablet (scored) OR 75/50/150 mg per 4 mL solution*	400 mg tablet OR 400 mg/8 mL solution#	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

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 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.

*** Continuation phase may be prolonged to 7 months in slow responders and children with HIV.

AND

- Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy:
 - Child < 5 years old: 12.5 mg.
 - Child ≥ 5 years old: 25 mg.

CHILDREN ≥ 8 YEARS AND ADOLESCENTS (AND ≥ 25 kg):

Note: The patient should be weighed regularly and the dose adjusted according to their current weight.

Body weight kg	2 months intensive phase given daily	4 months continuation phase given daily	
	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

AND

- Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy:
 - Child < 5 years old: 12.5 mg.
 - Child ≥ 5 years old: 25mg.

R=rifampicin, H=isoniazid, Z=pyrazinamide, E=ethambutol

C: DISSEMINATED (MILIARY) TUBERCULOSIS

Note: The 75/50 RH and 75/50/150 RHZ formulations are not suitable for achieving the required doses in disseminated TB & 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 (Rifampicin/Isoniazid)	Z (Pyrazinamide)	Eto (Ethionamide)
	60/60 mg dispersible tablet (scored)	500 mg tablet (scored) or 500 mg/8 mL suspension	250 mg tablet (scored) or 250 mg/8 mL suspension
<2 kg	Obtain Expert Advice		
2-2.9 kg	¼ 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
7-8.9 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		
17-17.9 kg	5 ½ tablets or 22 mL	1 ¼ tablets or 10 mL	1 ¼ tablet 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	

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

* If oral suspension 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 suspension

** 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

PLUS

- Pyridoxine 25 mg daily for 6 months.

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

D: TUBERCULOSIS MENINGITIS

Note: The 75/50 RH and 75/50/150 RHZ formulations are not suitable for achieving the required doses in disseminated TB & 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 (Rifampicin/Isoniazid)	Z (Pyrazinamide)	Eto (Ethionamide)
	60/60 mg dispersible tablet (scored)	500 mg tablet (scored) or 500 mg/8 mL suspension	250 mg tablet (scored) or 250 mg/8 mL suspension
<2 kg	Obtain Expert Advice		
2-2.9 kg	¼ 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
7-8.9 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		
17-17.9 kg	5 ½ tablets or 22 mL	1 ¼ tablets or 10 mL	1 ¼ tablet 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	

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

* If oral suspension 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 suspension

** 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

- » Consider prolonging treatment for another 3 months if there are concerns about ongoing disease.
- » Consult with a specialist.