



health

Department:
Health
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NOTICE: ETHIONAMIDE AVAILABILITY AND THERAPEUTIC ALTERNATIVE

The Paediatric Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) recommends the use of ethionamide in the regimens for the management of miliary tuberculosis (TB), and TB meningitis (TBM).

The available stock of ethionamide expired on 1 October 2024, and currently there is no other stock in the country to service this clinical need. The sourcing of ethionamide stock is currently underway, and supply is expected to resume in December 2024. Updates on availability and timelines will be shared as they become available.

In the interim, there are two alternative regimens (which exclude ethionamide) that may be considered for children with TBM or miliary TB, as tabulated below. These regimens may be considered both, for patients already on TB treatment who will be required to switch to an alternative regimen, as well as for newly diagnosed patients who need to be initiated on treatment. Consideration of regimen choice should be undertaken on a case-by-case basis in consultation with a specialist clinician. See *annexure 1 for dosing guidance*.

Regimen		Notes
World Health Organization (WHO) TBM regimen	12 month WHO regimen: 2RHZE + 10RH	This is the current regimen endorsed by the WHO (with dose adjustments, informed by guidance from local experts). The treatment duration is 12 months which may present a higher risk of non-completion for some patients.
Replacement of ethionamide with levofloxacin	6-month regimen: RHZ + levofloxacin	This is based on the existing 6-month regimen where ethionamide is replaced with levofloxacin and rifampicin is optimised. Note that this regimen is still investigational, so informed consent is required prior to initiation with close monitoring and follow up of patients.

R - rifampicin, H – isoniazid, Z- pyrazinamide, E - ethambutol

Provinces and Healthcare Facilities are requested to distribute and communicate this information in consultation with the Pharmaceutical and Therapeutics Committees. Kindly share with all healthcare professionals and relevant stakeholders.

Kind regards,

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DATE: 14 October 2024

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Annexure 1:

WHO REGIMEN

Body weight (kg)	Once daily; 7 days a week				Body weight (kg)		
	Intensive Phase (2 months)			Continuation phase (10 months)			
	Rifampicin/ Isoniazid (RH)*	Pyrazinamide (Z)	Ethambutol	Rifampicin/ Isoniazid (RH)*			
	75/50 mg dispersible tablet (scored)	500 mg tablet (scored) OR 500 mg/8 mL suspension**	400 mg tablet OR 400 mg/8 mL solution***	75/50 mg dispersible tablet (scored)			
< 2	Obtain Expert Advice				< 2		
2–2.9	¾ tablet or 3 mL	1 mL	1mL	¾ tablet or 3 mL	2–2.9		
3–3.9	1½ tablets or 6 mL	2 mL	1.5mL	1½ tablets or 6 mL	3–3.9		
4–4.9	< 3 months: 1 ½ tablets or 6 mL ≥ 3 months: 2 tablets or 8 mL	2.5 mL	2.5mL	< 3 months: 1 ½ tablets or 6 mL ≥ 3 months: 2 tablets or 8 mL	4–4.9		
5–5.9	2 ½ tablets or 10 mL	3 mL		2 ½ tablets or 10 mL	5–5.9		
6–7.9	3 tablets or 12 mL	½ tablet or 4 mL		3 tablets or 12 mL	6–7.9		
8–8.9	3 ½ tablets or 14 mL	¾ tablet or 6 mL	½ tablet or 4mL	3 ½ tablets or 14 mL	8–8.9		
9–9.9					9–9.9		
10–11.9	4 tablets or 16 mL	1 tablet or 8 mL	¾ tablet or 6mL	4 tablets or 16 mL	10–11.9		
12–12.9					12–12.9		
13–14.9	4 ½ tablets or 18 mL	1 tablet or 8 mL	1 tablet or 8mL	4 ½ tablets or 18 mL	13–14.9		
15–15.9	5 tablets or 20 mL			5 tablets or 20 mL	15–15.9		
16–16.9	6 tablets or 24 mL	1 ¼ tablets or 10 mL	1 tablet or 8mL	6 tablets or 24 mL	16–16.9		
17–17.9					17–17.9		
18–19.9					18–19.9		
20–24.9	7 tablets or 28 mL	1 ½ tablets or 12 mL		7 tablets or 28 mL	20–24.9		
25–29.9	Choose one option		2 tablets or 16 mL	1 ½ tablets or 12 mL	Choose one option	25–29.9	
30–34.9	RH 150/75 mg	RH 300/150 mg	2 ½ tablets or 20 mL		RH 150/75 mg RH 300/150 mg	30–34.9	
35–39.9	6 tablets	3 tablets	3 tablets or 24 mL	2 tablets or 16 mL	6 tablets	3 tablets	35–39.9
40–42.9			3 ½ tablets or 28 mL				40–42.9
43–49.9			4 tablets or 32 mL				2 ½ tablets or 20 mL
≥ 50							≥ 50

*If oral suspension required, for each dose, disperse 1 x RH 75/50 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.

***For ethambutol suspension, crush 1 tablet (400mg) to a fine powder and dissolve in 8ml of water to prepare a concentration of 400mg/8mL (or 50mg/mL). Give the child the required dose as indicated in the chart above and discard unused suspension.

REPLACEMENT OF ETHIONAMIDE WITH LEVOFLOXACIN

Body weight (kg)	Single phase of treatment, 6 months. Once daily; 7 days a week			Body weight (kg)	
	Rifampicin/Isoniazid (RH)*	Pyrazinamide (Z)	Levofloxacin		
	75/50 mg dispersible tablet (scored)	500 mg tablet (scored) OR 500 mg/8 mL suspension**	250 mg tablet OR 500 mg tablet OR 25 mg/ml suspension***		
< 2	Obtain Expert Advice			< 2	
2–2.9	¾ tablet or 3 mL	1 mL	2 mL	2–2.9	
3–3.9	1 ½ tablet or 6 mL	2 mL	3 mL	3–3.9	
4–4.9	< 3 months: 1 ½ tablets or 6 mL ≥ 3 months: 2 tablets or 8 mL	2.5 mL	4 mL	4–4.9	
5–5.9	2 ½ tablets or 10 mL	3 mL	5 mL or ½ x 250 mg tablet	5–5.9	
6–7.9	3 tablets or 12 mL	½ tablet or 4 mL	6 mL	6–7.9	
8–8.9	3 ½ tablets or 14 mL		7 mL	8–8.9	
9–9.9		4 tablets or 16 mL	¾ tablet or 6 mL	10 mL or 1 x 250 mg tablet	9–9.9
10–11.9	1 tablet or 8 mL		15 mL or 1 ½ x 250 mg tablet	10–11.9	
12–12.9				12–12.9	
13–14.9	4 ½ tablets or 18 mL	1 ¼ tablets or 10 mL	1 x 500 mg tablet or 2 x 250 mg tablet or 20 mL	13–14.9	
15–15.9	5 tablets or 20 mL			15–15.9	
16–16.9	6 tablets or 24 mL			17–17.9	
17–17.9		18–19.9			
18–19.9	7 tablets or 28 mL	1 ½ tablets or 12 mL	20–24.9		
20–24.9		2 tablets or 16 mL	1 ½ x 500mg or 3 x 250mg tablets daily	25–29.9	
25–29.9	<i>Choose one option</i>			25–29.9	
30–34.9	<i>RH 150/75 mg</i>	<i>RH 300/150 mg</i>	2 ½ tablets or 20 mL	30–34.9	
35–39.9	6 tablets	3 tablets	3 tablets or 24 mL	2 x 500mg or 4 x 250 mg tablets daily	35–39.9
40–49.9			3.5 tablets or 28 mL		40–49.9
≥ 50			4 tablets or 32 mL		≥ 50

*If oral suspension required, for each dose, disperse 1 x RH 75/50 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.
 ***For Levofloxacin 25mg/ml suspension: Crush and disperse 1 x 250mg tablet in 10 mL water.