

# Addendum to *Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Health Care Provider*

January 2014

## Overview

CDC has issued recommendations for the use of an additional treatment regimen for latent *M. tuberculosis* infection (LTBI).<sup>1</sup> The new regimen combines isoniazid (INH) and rifapentine (RPT) and is given in 12 once-weekly doses using directly observed therapy (DOT). This regimen must be provided via DOT because missed doses, altered dosing intervals or amounts, or incomplete treatment could jeopardize the 12-dose regimen efficacy or safety.

The 12-dose once-weekly regimen is recommended as an option equal to the standard INH 9-month daily regimen for treating LTBI in otherwise healthy people, 12 years of age and older, who were recently in contact with infectious TB, or who had tuberculin skin test or blood test for TB infection conversions. It is an additional LTBI treatment option and does not replace the other options for LTBI treatment<sup>2</sup> (see Table 1). The 12-dose regimen can be considered for other groups when it offers practical advantages, such as treatment completion within a limited timeframe. The preferred regimen for children 2-11 years is 9 months of daily INH. However, the 12-dose INH-RPT regimen can be considered on a case by-case basis in this population when both 1) the circumstances make the completion of 9 months of daily INH unlikely and 2) the likelihood of developing TB or the potential severity is great (e.g., recent *M. tuberculosis* infection in a preschool-aged child).

The 12-dose regimen is NOT recommended for:

- Children younger than 2 years of age
- People with HIV/AIDS who are taking antiretroviral treatment
- People who are known or presumed to have been infected with INH or rifampin (RIF) resistant *M. tuberculosis*
- Pregnant women, including adolescents, or women expecting to become pregnant while taking this regimen.

The choice between the 12-dose once-weekly regimen and other approved LTBI treatment regimens depends on several factors, including the feasibility of DOT, resources for drug procurement and patient monitoring, medical and social circumstances of the patient that may affect treatment completion and, preferences of the patient and the prescribing physician. When choosing a regimen for LTBI, consider possible significant rifampin-associated drug interactions including, but not limited to hormonal contraceptives, antiretrovirals, and anticoagulants. Use of a non-hormonal birth-control method is recommended when rifampin or rifapentine is administered to a sexually active female.

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## References

1. CDC. Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. *MMWR* 2011;60:1650-1653.  
[http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s\\_cid=mm6048a3\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w)
2. ATS/CDC. Targeted tuberculin testing and treatment of latent TB infection. *MMWR* 2000;49(No. RR- 6).  
<http://www.cdc.gov/MMWR/PDF/rr/rr4906.pdf>

**Table 1: Options for the Treatment of Latent TB Infection** <sup>1,2</sup>

Drug(s)	Duration	Dose	Interval	Minimum Doses
Isoniazid (INH)	9 months	Adult: 5 mg/kg Children: 10-20 mg/kg* Maximum dose: 300 mg	Daily	270
		Adult: 15 mg/kg Children: 20-40 mg/kg* Maximum dose: 900 mg	Twice weekly†	76
	6 months	Adult: 5 mg/kg Children: Not recommended Maximum dose: 300 mg	Daily	180
		Adult: 15 mg/kg Children: Not recommended Maximum dose: 900 mg	Twice weekly†	52
Isoniazid (INH) and Rifapentine (RPT)	3 months	Adults and Children 12 and over** INH:*** 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT:*** 10.0–14.0 kg 300 mg 14.1–25.0 kg 450 mg 25.1–32.0 kg 600 mg 32.1–49.9 kg 750 mg ≥50.0 kg; 900 mg maximum	Once weekly†	12
Rifampin (RIF)	4 months	Adults only: 10 mg/kg Maximum dose: 600 mg	Daily	120
	6 months	For children 10-20 mg/kg****	Daily	180

\* The American Academy of Pediatrics recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.

\*\* Can be considered on a case-by-case basis for children 2-11 years (See text)

\*\*\* Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifapentine (RPT) is formulated as 150 mg tablets in blister packs that should be kept sealed until used.

\*\*\*\* For the treatment of LTBI in infants, children and adolescents *when* INH cannot be tolerated *or* if the child has had contact with a patient infected with an INH resistant, but rifampin susceptible organism.

† Intermittent regimen must be provided via directly observed therapy (DOT), i.e., health care worker observes the ingestion of medication.

### Possible adverse reactions to the 12-dose regimen

Adverse drug reactions in children are uncommon.

***Isoniazid:*** Hepatitis/hepatotoxicity (symptoms include nausea, vomiting, abdominal pain, anorexia, yellow eyes/skin, light stools, dark urine), rash, peripheral neuropathy, hypersensitivity, mild CNS effects

***Rifapentine:*** Hepatitis/hepatotoxicity (symptoms include nausea, vomiting, abdominal pain, anorexia, yellow eyes/skin, light stools, dark urine), hypersensitivity reactions (may include rash, dizziness, hypotension and flu-like symptoms, such as fever, muscle aches and headache), thrombocytopenia, neutropenia evidenced by easy bruising or bleeding, and orange discoloration of body fluids and soft contact lenses.

Report adverse events through MedWatch (FDA Adverse Event Reporting Program) at:

<http://www.fda.gov/Safety/MedWatch/default.htm> and by sending an email to the CDC National Surveillance for Severe Adverse Events Project at [ltbidruevents@cdc.gov](mailto:ltbidruevents@cdc.gov)

### Additional Resources:

CDC website: <http://www.cdc.gov/tb>

Patient education brochure: [http://www.cdc.gov/tb/publications/PDF/3HP\\_508.pdf](http://www.cdc.gov/tb/publications/PDF/3HP_508.pdf)