

Virginia Department of Health

Use of Isoniazid/Rifapentine for Treatment of Latent TB Infection in Health Department Settings

The identification and treatment of latent tuberculosis infection (LTBI) is a cornerstone of the U.S. strategy for the elimination of tuberculosis. In 2018, the Centers for Disease Control and Prevention (CDC) updated recommendations for the treatment of LTBI using a once-weekly regimen of isoniazid (INH) and rifapentine (RPT).¹ This regimen offers practical advantages with clients who are unlikely to complete 9 months of daily INH or in settings such as correctional facilities, homeless shelters and clinics for recent immigrants where the regimen may offer practical advantages.

These recommendations are an adjunct to already published guidelines on the diagnosis and treatment of latent tuberculosis that were published in 2000³ and the 2011 recommendations.²

Recommendations for regimens detailed in the previous guidelines for treating LTBI are unchanged and remain treatment options for any client. The recommendation of two months of rifampin/pyrazinamide recommended in the 2000 guidelines was later withdrawn due to increased risk of hepatotoxicity and death.⁴

Recommendations

1. INH-RPT can be considered for the treatment of LTBI in healthy patients ≥ 2 years of age after active disease has been adequately ruled out.
 - a. This includes those with recent exposure, recent conversion from negative to positive on a test for LTBI, and those with radiographic findings of healed TB as long as active disease has been adequately ruled out.
2. The regimen can be considered for HIV-infected patients who are not taking anti-retroviral medications as well as those taking antiretroviral medications with acceptable drug-drug interactions with Rifapentine.
3. The regimen consists of a once weekly dose of both medications given for twelve weeks.
VDH advocates for the regimen to be given by Directly Observed Therapy (DOT).
 - a. The choice of this regimen is based on the feasibility of directly observed therapy (DOT), resources for obtaining the drugs, client monitoring, expectation of treatment completion and preferences of the client and prescriber.
 - b. Completion of this regimen is defined as 11 or 12 doses within 16 weeks.
 - c. Doses should be separated by >72 hours to be countable.
 - d. Dosing information is provided in Table 1.
4. INH-RPT is **NOT** recommended for:
 - a. Children < 2 years of age
 - b. HIV-infected clients receiving antiretrovirals that have drug-drug interactions with rifapentine
 - c. Pregnant women or those likely to become pregnant while undergoing treatment
 - d. Clients with LTBI presumed to be INH or rifampin resistant

5. Other Considerations

- a. Rifapentine, like rifampin and rifabutin, has the potential to cause many drug-drug interactions due to its effects of inducing a variety of metabolic pathways, particularly those involving the cytochrome P450 system. This results in a decrease in the serum concentrations of many drugs, sometimes to sub-therapeutic levels.
- b. Rifapentine is considered an intermediate enzyme inducer while rifampin is a potent inducer and rifabutin is the least potent inducer.
- c. Before recommending the INH/rifapentine for any given client, a careful review of all current medications, both prescription and over the counter (OTC) with a reference search for potential drug-drug interactions should be undertaken.
- d. Clients should be questioned during each DOT visit concerning new prescription and OTC medication additions since the last visit.

6. Monitoring

- a. Clients should be taught the symptoms of adverse reactions to the medications and to seek medical attention should symptoms occur.
- b. If clients report symptoms of adverse reactions, they should receive an immediate clinical assessment and monitoring.
- c. Clients should be questioned at each DOT visit regarding symptoms of adverse reactions. Maintain vigilance for hypersensitivity reactions, especially hypotension or thrombocytopenia.
- d. Monthly clinical assessment for side effects including brief physical examination for hypotension, jaundice, tenderness of liver, or rashes.
- e. Baseline liver function tests (ALT, AST, TBili, Alk phos), for the following clients:
 - i. HIV-infected clients
 - ii. Clients with liver disorders
 - iii. Clients in the immediate postpartum i.e. ≤ 3 months after delivery
 - iv. Clients with regular alcohol usage, or injection drug use
 - v. Baseline testing for older clients, especially those on other hepatotoxic medications, should be considered on a case by case basis.
- f. Monthly monitoring of LFTs is not necessary unless baseline testing is abnormal or the client is at risk for liver disease.
- g. Discontinue medication if the AST is ≥ 5 times upper limit of normal in the absence of symptoms or ≥ 3 times the upper limit of normal in the presence of hepatotoxic symptoms.
- h. Adverse reactions leading to hospital admission or death should be reported to VDH TB Control at 804-864-7906 for further reporting to the CDC.

Table 1 – Dosing

Drug	Dosage	Maximum dose
INH	15 mg/kg rounded to nearest 50/100 mg in patients ≥ 12 years	900 mg
	25 mg/kg rounded ⁵ to the nearest 50/100 mg in patients 2-11 years	
Rifapentine	10.0 – 14.0 kg = 300 mg	900 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 max	
Rifapentine tablets can be crushed and administered with semi-solid food for children unable to swallow pills		

¹Centers for Disease Control and Prevention. Update of Recommendations for Use of Once - Weekly Isoniazid-Rifapentine Regimen Treat latent *Mycobacterium tuberculosis* Infection. MMWR 2018;67(25):723-726. <https://www.cdc.gov/mmwr/volumes/67/wr/mm6725a5.htm>

²Centers for Disease Control and Prevention. 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/pdf/wk/mm6048.pdf>

³Centers for Disease Control and Prevention. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000;49 (No. RR-6) <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>

⁴Centers for Disease Control and Prevention. Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection – United States, 2003. MMWR 2003; 52:735-739. <http://www.cdc.gov/mmwr/PDF/wk/mm5231.pdf>

⁵Cruz AT and Starke JR. Completion Rate and Safety of Tuberculosis Infection Treatment With Shorter Regimens. *Pediatrics*. 2018;141(2):e20172838