

**Provider Guidance Fact Sheet:
12-dose Isoniazid (INH)/Rifapentine Regimen for Latent TB Infection Treatment**

NOTE: It is imperative to rule out active disease in all persons prior to initiating treatment for LTBI

How many are infected with tuberculosis?

In Virginia, it is estimated that 2.8% of the population have tuberculosis (TB) infection. In 2019 latent TB infection (LTBI) will be a reportable condition for all ages. In 2017, 204 persons were diagnosed with TB disease in Virginia. An essential element of TB control is the treatment of latent TB infection.

What is the 12-dose INH/rifapentine 3HP regimen?

It consists of 12 once-weekly doses of INH and rifapentine administered by directly observed therapy (DOT) for the treatment of LTBI.

Is the regimen effective?

Randomized controlled trials in adults¹ and children² showed that the 12-dose regimen administered by DOT is as effective as 9 months of daily INH self-administered therapy (SAT) for LTBI treatment. The 12-dose regimen was more likely to be completed when compared to 9 months of daily INH.^{1,2}

What are the advantages of this regimen?

- The 12-dose regimen reduces treatment time by two-thirds (from 9 months to 3 months)
- Weekly dosing offers convenience
- Higher rates of treatment completion
- Lower rates of hepatotoxicity

Who should be considered for treatment with the 12-dose regimen for LTBI?

- 3HP is recommended for treating LTBI in persons age 2 and older who do not take medications that interact with Rifapentine
- Short course regimens are preferred whenever possible to enhance the likelihood of LTBI treatment completion

Who is NOT recommended for treatment with the 12-dose regimen?

- Children under 2 years of age
- HIV infected persons taking certain antiretrovirals (potential drug interactions between rifapentine and antiretrovirals)
- Individuals taking medications that may have drug interactions that are difficult to manage with the 12-dose regimen

- Persons presumed infected with *M. tuberculosis* resistant to INH or rifampin
- Pregnant women or women planning to become pregnant during treatment
- Individuals who have had prior adverse events or hypersensitivity to INH or rifampin

What are the doses?

Drug	Dosage	Maximum dose
INH	15 mg/kg rounded to nearest 50/100 mg in patients ≥ 12 years	900 mg
	25 mg/kg rounded 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	
Rifapentine tablets can be crushed and administered with semi-solid food for children unable to swallow pills		

What is completion of therapy?

Completion of therapy is defined in the study as completing at least 11 weekly doses of treatment within 16 weeks. Doses should be given at least 72 hours apart.

Does this regimen have to be administered via DOT?

- The Virginia Department of Health (VDH) recommends the use of DOT to ensure treatment adherence and completion
- A CDC-sponsored trial recently investigated SAT of 3HP and evidence supports that SAT is non-inferior to DOT of 3HP for treatment in the United States³
- As a result of this data many clinicians are applying SAT or modified DOT approaches with 3HP
- Clinicians may choose to provide 3HP by SAT or DOT based on individual risk and need

How frequently were toxicities observed in the 12-dose regimen in the clinical trial participants?

- Possible hypersensitivity (3.8%)
- Rash (0.8%)
- Hepatotoxicity (0.4%)
- Thrombocytopenia (infrequent)
- Other toxicities (3.2%)

Note: Refer to product insert for full list of side effects.

What can a hypersensitivity reaction include and how should I respond?

Hypersensitivity reactions may include a flu-like syndrome (e.g., fever, chills, headaches, dizziness, musculoskeletal pain), thrombocytopenia, shortness of breath or other signs and symptoms including wheezing, acute bronchospasm, urticaria, petechiae, purpura, pruritus, conjunctivitis, angioedema, hypotension or shock.

- If moderate to severe reaction (e.g., thrombocytopenia, hypotension, syncope), hospitalization or life-threatening event ➡ Discontinue treatment
- If mild reaction (e.g., rash, dizziness, fever) ➡ Continue to monitor patient closely with a low threshold for discontinuing treatment

How do I report an adverse event regarding the 12-dose regimen?

All adverse events should be reported to [FDA MedWatch](https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm), (<https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>)

Report adverse events leading to death or hospitalization to the local health department, who will report to VDH.

Final Recommendations:

- At completion of treatment, provide client with documentation of their TB test, chest x-ray results, medication treatment regimen and duration of treatment.

For questions, contact the VDH TB Control Program at 804-864-7906.

Resources

[Virginia Department of Health
Tuberculosis Control Program](http://www.vdh.virginia.gov/tuberculosis-and-newcomer-health)

www.vdh.virginia.gov/tuberculosis-and-newcomer-health
804-864-7906

[Centers for Disease Control and Prevention Division
of Tuberculosis Elimination](http://www.cdc.gov/tb/) <http://www.cdc.gov/tb/>
800-232-4636

[FDA MedWatch](https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm)

<https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>
888-463-6332

Are there drug-drug interactions?

- INH increases blood levels of phenytoin and disulfiram
- Rifapentine decreases blood levels of oral contraceptives, warfarin, sulfonylureas, methadone, steroids, some cardiac medications, and some antibiotics including fluoroquinolones
- Rifapentine has interactions similar to rifampin; it induces cytochromes P4503A4 & P4502C8/9 (less than rifampin)

Note: Refer to product insert for full list of interactions.

What type of monitoring do I need to do?

- Monthly interview and brief physical examination to identify treatment-associated adverse events
- Baseline hepatic chemistry is recommended for patients with specific conditions:
 - HIV infection
 - Liver disorders
 - In the immediate postpartum period
 - Regular alcohol use
 - Consider also for older persons and those taking medications for chronic medical conditions
- If baseline hepatic chemistry testing is abnormal, continue with subsequent testing

Adapted from LA County DOH, April 2017