

## 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 California, an estimated 2.4 million people have tuberculosis (TB) infection. In 2015, 2,137 persons were diagnosed with TB disease in California. An essential element of TB control is the treatment of latent TB infection (LTBI).

### What is the 12-dose INH/rifapentine 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 adults<sup>1</sup> and children<sup>2</sup> 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.<sup>1,2</sup>

### 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?

- The 12-dose regimen is recommended as an equal alternative to 9 months of daily INH by SAT for treating LTBI
- 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 antiretrovirals (there are potential drug interactions with 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 $\geq$ 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?

- A CDC-sponsored trial recently investigated SAT of 3HP and preliminary data suggests that SAT is non-inferior in the United States<sup>3</sup>
- As a result of this data many clinicians are applying SAT or modified DOT approaches with 3HP
- As of 2011 the CDC recommends DOT for this regimen, but future national guidance will likely reflect the newer data

### 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>

Report adverse events leading to death or hospitalization to the local health department, who will report to the CDPH TB Control Branch (TBCB). TBCB then reports to the CDC.

**Are there drug-drug interactions?**

- INH increases blood levels of phenytoin and disulfiram
- Rifapentine decreases blood levels of oral contraceptives, warfarin, sulfonyleureas, 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.

**For questions or assistance in accessing rifapentine, contact the TB Control Branch at 510-620-3000.**

**Resources**

California Department of Public Health  
Tuberculosis Control Branch (TBCB)  
<http://www.cdph.ca.gov/programs/tb/Pages/default.aspx>  
510-620-3000

**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

**What is the approximate monthly public health pricing cost of the 12-dose regimen?**

Rifapentine & INH	\$ 22.60 + \$1.00
Monthly clinic visit	\$ 26.00
DOT	\$ 96.00
<b>TOTAL</b>	<b>\$147.00 monthly</b>

**How do I obtain Medi-Cal reimbursement?**

- Use the ICD-10 codes for tuberculosis infection
- Rifapentine is reimbursed at approximately \$20.00 per 900 mg dose
- DOT is reimbursed at approximately \$19.00 per encounter
- Instructions for Medi-Cal DOT reimbursement [www.medi-cal.ca.gov](http://www.medi-cal.ca.gov)

**How do I get rifapentine for my program?**

Rifapentine can be ordered from your distributor or wholesaler, or directly from the manufacturer, Sanofi-Aventis, at [www.sanofi.us](http://www.sanofi.us) and can be found in the “other products” link.

California TB Controllers Association  
<http://www.ctca.org/>  
510-479-6139

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

Curry International Tuberculosis Center  
Warmline Consultation Service  
<http://www.currytbcenter.ucsf.edu/>  
877-390-6682 or 510-238-5100

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

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## References

1. Sterling, T., Villarino, M., Borisov, A., et al. (2011). Three months of rifapentine and isoniazid for latent tuberculosis infection. *The New England Journal of Medicine*, 365(23). 2155-2166.
2. Villarino, M., Scott N., Weis, S., et al. (2015). Treatment for Preventing Tuberculosis in Children and Adolescents. *JAMA Pediatrics*, 169(3):247-255.
3. Belknap, R., Borisov, A., Holland, D., et al. (2015). Adherence to Once-Weekly Self-Administered INH and Rifapentine for Latent TB: Adhere. [Abstract 827LB CROI, 2016].
4. Centers for Disease Control and Prevention. (2011). *Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent mycobacterium tuberculosis infection*. (MMWR Vol. 60 No. 48). Georgia: U.S. Department of Health and Human Services.
5. Holland, D., Sanders, G., Hamilton, C., and Stout, J. (2011). Potential economic viability of two proposed rifapentine-based regimens for treatment of latent tuberculosis infection. *Public Library of Science ONE*, 6(7). E22276.
6. Martinson, N., Barnes, G., Moulton, L., et al. (2011). New regimens to prevent tuberculosis in adults with HIV infection. *New England Journal of Medicine*, 365. 11-20.
7. Schechter, M., Zajdenverg, R., Falco, G., et al. (2006). Weekly rifapentine/isoniazid or daily rifampin/pyrazinamide for latent tuberculosis in household contacts. *American Journal of Respiratory Critical Care Medicine*, 173. 922-926.
8. Sterling, TR., Moro, RN., Borisov, AS., et al. (2015). Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT tuberculosis study. *Clinical Infectious Diseases*, 61 (4). 527-535.