

12-dose Isoniazid (INH) + rifapentine Regimen for the Treatment of TB Infection

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

What is the 12-dose INH + rifapentine regimen?

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

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 TB infection treatment, which is estimated to be about 90% effective. 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 the 12-dose 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
- Substantially lower rates of hepatotoxicity

Who should be considered for treatment with this regimen?

- The 12-dose regimen is recommended as an equal alternative to 9 months of daily INH by SAT for treating TB infection
- Short course regimens are preferred whenever possible to enhance the likelihood of TB infection 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 rifamycins.

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

Does this regimen have to be administered via DOT?

- As of 2011, the CDC recommends DOT for this regimen; subject to change pending new data
- A CDC-sponsored trial investigated SAT of 3HP and preliminary data suggests that SAT is non-inferior in the United States³
- As a result of this data many clinicians are applying SAT or modified DOT approaches with 3HP
- **LAC TBCP recommends that the 12-dose regimen be administered via DOT until the clinician becomes experienced with its potential side-effects before administering this regimen via SAT**

What are the possible side effects?

- 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.

12-dose INH + rifapentine Regimen for the Treatment of TB infection — *continued*

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, wheezing, acute bronchospasm, urticaria, petechiae, purpura, pruritus, conjunctivitis, angioedema and 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 then report to the CDPH TB Control Branch (TBCB). TBCB then reports these events to the CDC.

Are there drug-drug interactions?

- INH increases blood levels of phenytoin and disulfiram
- Rifapentine decreases blood levels of numerous drugs (e.g., transplantation drugs, oral contraceptives, warfarin, sulfonyleureas, opioids, steroids, antihypertensives, etc.).
- Rifapentine has interactions similar to rifampin; it induces cytochromes P4503A4 & P4502C8/9 (less than rifampin)

NOTE: refer to product insert and/or pharmacological reference 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 at least monthly testing as indicated.

What is completion of therapy?

- Defined as completing at least 11 weekly doses of treatment within 16 weeks. Doses should be given at least 72 hours apart.

What should be done when treatment is completed?

- Patients should receive written documentation of TST or IGRA testing results, CXR results, names and dosages of medications, and duration of treatment anytime TB testing is requested.
- Providers should re-educate patients about the signs and symptoms of TB reactivation and advise them to contact a medical provider if these symptoms develop.
- Repeat CXR's are not indicated unless TB symptoms or TB disease is suspected.

What is the approximate public health (340B pricing) drug costs of the 12-dose regimen?

INH + rifapentine	\$3 + \$69
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How do I obtain Medi-Cal reimbursement?

- Use the ICD-10 codes for TB infection
- Rifapentine is reimbursed at approximately \$20 per 900 mg dose
- For public health providers, DOT is reimbursed at approximately \$19 per encounter

How do I get rifapentine for my program or clinic?

Rifapentine can be ordered directly from your distributor or wholesaler, or directly from the manufacturer, Sanofi-Aventis, at www.sanofi.us

Resources

Los Angeles County TB Control Program <http://www.publichealth.lacounty.gov/tb>
213-745-0800

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

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.fda.gov/Safety/MedWatch/default.htm>

