



12-dose Isoniazid (INH) + Rifapentine Regimen for Latent TB Infection (LTBI) Treatment



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

What is the 12-dose INH+rifapentine regimen?

An LTBI treatment regimen consisting of 12 once-weekly doses of INH and rifapentine. This is a preferred LTBI treatment regimen because it is a short-course treatment with higher completion rates.

Is the regimen effective?

Randomized controlled trials in adults and children showed that the 12-dose regimen administered by DOT is as effective as 9 months of daily INH by SAT for LTBI treatment. The 12-dose regimen was more likely to be completed when compared to 9 months of daily INH.

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 that have unacceptable drug interactions with rifapentine
- Persons 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 or breastfeeding women or women planning to become pregnant during treatment
- Persons 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 up to nearest 50/100 mg in patients ≥12 years	900 mg
	25 mg/kg rounded up 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 – 50 kg = 750 mg	
	> 50 kg = 900 mg	

*Rifapentine and INH tablets can be crushed and administered with semi-solid food for patients unable to swallow pills

What is completion of therapy?

Completion of therapy is 12 doses in 16 weeks. In situations where 12 doses cannot be completed, at least 11 weekly doses of treatment within 16 weeks can be considered complete. Doses must be given at least 72 hours apart.

Does this regimen have to be administered via DOT?

- CDC recommends either SAT or DOT in persons aged ≥2years
- DOT vs SAT should be based on local practice, individual patient characteristics and preferences considering the following:
 - The burden and expense of DOT on patients and providers is greater than for SAT.
 - In a randomized trial of INH+rifapentine completion, SAT has been shown to be non-inferior to DOT among adults in the United States.
 - DOT may be beneficial for patients in whom risk for progression to severe forms of active TB disease if adherence is poor. Examples include age less than 5 years and immunosuppression.
- Contact your local TB control program regarding local recommendations.



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%)
- Refer to product insert for full list of side effects

What is a hypersensitivity reaction and how should I respond?

Hypersensitivity reactions may include a flu-like syndrome (e.g., fever, chills, headaches, dizziness, and 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: 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 carbamazepine and some benzodiazepines.
- Rifapentine decreases blood levels of many drugs including hormonal contraceptives, warfarin, sulfonyleureas, methadone, steroids, some cardiac medications, and some antibiotics including fluoroquinolones
- Rifapentine has interactions similar to rifampin; it induces cytochromes P450 3A4 & P450 2C8/9 (less than rifampin)
- Refer to product insert or other drug interaction resource 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 is ideal. Telephone or other patient communication can also encourage adherence and identify problems.

- Baseline hepatic chemistry is recommended for patients with specific conditions:
 - HIV infection
 - Liver disorders
 - In the immediate (within 3 months) 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 and consider viral hepatitis testing.

How do I get rifapentine?

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

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

Resources

California Department of Public Health Tuberculosis Control Branch (TBCB): cdph.ca.gov/tbcb

California TB Controllers Association: ctca.org

CDC Division of Tuberculosis Elimination: cdc.gov/tb

Curry International Tuberculosis Center Consultation currytbcenter.ucsf.edu/consultation or (877) 390-6682

Abbreviations

AFB= acid-fast bacilli BCG= Bacillus Calmette-Guérin
CXR= chest x-ray DOT= directly observed therapy
IGRA=interferon gamma release assay LTBI= latent TB infection
MDR =multiple drug resistant NAAT= nucleic acid amplification testing
SAT= self-administered therapy TST= tuberculin skin test

