



# TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI)

## WITH REVISED GUIDELINES FOR RIF-PZA

CHARLES P. FELTON NATIONAL TUBERCULOSIS CENTER AT HARLEM HOSPITAL

Samuel L. Kountz Pavilion • 15 West 136th Street • Sixth Floor • New York, NY 10037 • phone (212) 939-8254 • fax (212) 939-8259 • <http://harlemtbcenter.org>

### WHO TO TEST

Target tuberculin skin testing (TST) at persons at high risk for TB:

- Persons at risk for recent *M. tb* infection
- Persons at risk for progression to active TB

Treat LTBI—it benefits the individual and the community.

Adherence is the key to successful prevention.

### WHO TO TREAT

CATEGORY OF PERSON TESTED	TST <5 mm	TST ≥5 mm	TST ≥10 mm	TST ≥15 mm
Child <5 years and recent contact*	TREAT	TREAT	TREAT	TREAT
HIV-infected and recent contact*	TREAT	TREAT	TREAT	TREAT
Immunosuppressed and recent contact*	TREAT	TREAT	TREAT	TREAT
HIV-infected	Do Not Treat	TREAT	TREAT	TREAT
Immunosuppressed persons	Do Not Treat	TREAT	TREAT	TREAT
Recent contact of TB case	Do Not Treat	TREAT	TREAT	TREAT
Fibrotic changes on chest X-ray	Do Not Treat	TREAT	TREAT	TREAT
Recent arrival from endemic country	Do Not Treat	Do Not Treat	TREAT	TREAT
Injection drug user	Do Not Treat	Do Not Treat	TREAT	TREAT
Resident/Employee institutional setting <sup>§</sup>	Do Not Treat	Do Not Treat	TREAT	TREAT
Mycobacteria lab personnel	Do Not Treat	Do Not Treat	TREAT	TREAT
High-risk clinical conditions <sup>‡</sup>	Do Not Treat	Do Not Treat	TREAT	TREAT
Child <4 years	Do Not Treat	Do Not Treat	TREAT	TREAT
Persons <18 exposed to high-risk adults	Do Not Treat	Do Not Treat	TREAT	TREAT
No risk factors (TST discouraged)	Do Not Treat	Do Not Treat	Do Not Treat	Consider Treating

\* Contacts should receive a tuberculin skin test (TST) immediately. Even if TST is 00mm, these groups should be treated and TST placed again 12 weeks after last exposure to TB case. Treatment can be discontinued in a healthy child if second TST is negative.

§ TST Conversion: An increase in reaction size of ≥10 mm within 2 years should be considered a TST conversion indicative of recent infection with *M. tb*.

‡ Silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g. leukemias and lymphomas), other specific malignancies (e.g. carcinoma of the head and neck or lung), weight loss of ≥10% of ideal body weight, gastrectomy, jejunioileal bypass.

Pregnancy: Treat during pregnancy if either HIV-infected or recent *M. tb* infection.

### HOW TO TREAT

Drug	Interval and Duration	Adult Dosage (max)	Criteria for Completion	Comments
INH	Daily for 9 mos.	5 mg/kg (300 mg)	270 doses within 12 mos.	<b>Preferred regimen for all persons.</b> INH may be administered concurrently with NRTIs, protease inhibitors, or NNRTIs. <b>DOT must be used with twice-weekly dosing.</b>
	Twice-weekly for 9 mos.	15mg/kg (900 mg)	76 doses within 12 mos.	
INH	Daily for 6 mos.	5 mg/kg (300 mg)	180 doses within 9 mos.	Not indicated for persons with HIV infection or fibrotic lesions, or for children. <b>DOT must be used with twice-weekly dosing.</b>
	Twice-weekly for 6 mos.	15mg/kg (900 mg)	52 doses within 9 mos.	
RIF*	Daily for 4 mos.	RIF 10 mg/kg (600 mg)	120 doses within 6 mos.	For contacts of patients with INH-resistant, RIF-susceptible TB.
RIF* plus PZA	Daily for 2 mos.	RIF 10 mg/kg (600 mg) PZA 15-20 mg/kg (2.0 g)	60 doses within 3 mos.	<b>Generally should not be offered</b> for treatment of LTBI for HIV-infected or HIV-negative persons. Consider use when completion of longer treatment courses is unlikely and when patients can be monitored closely. Consult TB/LTBI expert. Inform patients of potential hepatotoxicity and advise against use of potentially hepatotoxic agents, e.g. acetaminophen. Dispense no more than a 2-week supply. <b>DOT must be used with twice-weekly dosing.</b>
	Twice-weekly for 2-3 mos	RIF 10 mg/kg (600 mg) PZA 50 mg/kg (4.0g)	16-26 doses within 3-4 mos.	

Abbreviations: INH = isoniazid, RIF = rifampin, PZA = pyrazinamide, NRTIs = nucleoside reverse transcriptase inhibitors, NNRTIs = non-nucleoside reverse transcriptase inhibitors, DOT = directly observed therapy, mos. = months  
 Pregnancy: INH regimens preferred for pregnant women. PZA should be avoided during first trimester.

MDR-TB exposure: For persons who are likely to be infected with INH and RIF (multidrug) resistant-TB and at high risk of reactivation, PZA and ethambutol or PZA and a quinolone for 6-12 months are recommended. (Consult expert.)

\* HIV co-infection: Protease inhibitors or NNRTIs should not be administered concurrently with RIF; an alternative is rifabutin 300 mg daily. Rifabutin should not be used with hard-gel saquinavir or delavirdine. Dose adjustment of rifabutin may be required: to 150 mg twice-weekly with ritonavir or lopinavir/ritonavir, to 150 mg daily or 300 mg twice-weekly with other protease inhibitors, or to 450-600 mg daily or 600 mg twice-weekly with efavirenz.

### HOW TO MONITOR

#### For all patients:

- Initial clinical evaluation, including radiologic studies to rule out active TB
- Consider possible rifamycin-associated drug interactions, eg. oral contraceptives, antiretrovirals, methadone, oral hypoglycemics, and anticoagulants
- Provider conversant in patient's language should educate patients about side effects associated with LTBI treatment and advise to stop treatment and promptly seek medical evaluation if these occur
- Follow-up evaluations at least monthly if receiving INH or RIF alone; at 2, 4, 6, and 8 weeks if receiving RIF and PZA
- Include careful questioning about side effects and a brief physical examination checking for evidence of hepatitis or other side effects
- Inform persons considering treatment with RIF-PZA of potential hepatotoxicity and ask about history of liver disease or adverse effects from INH or other drugs

- If side effects occur, evaluate promptly and change treatment as indicated
- Routine monthly monitoring of liver function tests (LFTs) not generally indicated, except in the following circumstances:
  - Abnormal LFT at baseline
  - Chronic liver disease
  - HIV infection
  - Regular alcohol use
  - Pregnancy or immediate postpartum
  - RIF-PZA regimen

#### Medication should be withheld and patients evaluated if:

- Transaminase levels >3 times upper limit of normal in presence of symptoms
- Transaminase levels >5 times upper limit of normal in asymptomatic patient
- In patients on RIF-PZA: transaminase levels > normal if symptomatic, or if bilirubin > normal even if asymptomatic.