



# TREATMENT OF LTBI: LATENT TUBERCULOSIS INFECTION

## WITH REVISED GUIDELINES FOR RIF-PZA

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### 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 <sup>§</sup>	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	TREAT

\* 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.

<sup>§</sup> 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*.

<sup>‡</sup> 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 months	5 mg/kg (300 mg)	270 doses within 12 months	Preferred regimen for all persons. Use for HIV-infected persons when completion of treatment can be assured. INH may be administered concurrently with NRTIs, protease inhibitors, or NNRTIs.
	Twice-weekly for 9 months	15mg/kg (900 mg)	76 doses within 12 months	DOT must be used with twice-weekly dosing.
INH	Daily for 6 months	5 mg/kg (300 mg)	180 doses within 9 months	Not preferred for persons with HIV infection or fibrotic lesions. Not indicated for children.
	Twice-weekly for 6 months	15mg/kg (900 mg)	52 doses within 9 months	DOT must be used with twice-weekly dosing.
RIF*	Daily for 4 months	RIF 10 mg/kg (600 mg)	120 doses within 6 months	Alternate to longer regimens; also for contacts of patients with INH-resistant, RIF-susceptible TB.
RIF plus PZA	Daily for 2 months	RIF 10 mg/kg (600 mg) PZA 15-20 mg/kg (2.0 g)	60 doses within 3 months	Use when completion of longer treatment courses is unlikely and when patients can be monitored closely; also for contacts of patients with INH-resistant, RIF-susceptible TB. Use with caution in patients on hepatotoxic agents or with history of alcoholism. NOT recommended for persons with liver disease or with INH-associated liver injury. Dispense no more than a 2-week supply of RIF-PZA to facilitate periodic clinical assessments.
	Twice-weekly for 2-3 months	RIF 10 mg/kg (600 mg) PZA 50 mg/kg (4.0g)	16-26 doses within 3-4 months	DOT must be used with twice-weekly dosing.

**Abbreviations:** INH = isoniazid, RIF = rifampin, PZA = pyrazinamide, NRTIs = nucleoside reverse transcriptase inhibitors, NNRTIs = non-nucleoside reverse transcriptase inhibitors, DOT = directly observed therapy

**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

- 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
- 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
  - HIV infection
  - Pregnancy or immediate postpartum
  - Chronic liver disease
  - Regular alcohol use
  - 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.