

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

* All pregnant and breast-feeding women taking INH should receive pyridoxine (B₆) supplementation.

† 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 delamanvir. 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.

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). Avoid PZA during first trimester.

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.	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. DOT must be used with twice-weekly dosing.
	Twice-weekly for 9 mos.	15 mg/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.
	Twice-weekly for 6 mos.	15 mg/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.
	Daily for 2 mos.	RIF 10 mg/kg (600 mg) PZA 15-20 mg/kg (2.0 g)	60 doses within 3 mos.	
RIF plus PZA‡	Daily for 2 mos.	RIF 10 mg/kg (600 mg) PZA 50 mg/kg (4.0g)	16-26 doses within 3-4 mos.	Inform patients of potential hepatotoxicity and advise against use of potentially hepatotoxic agents, e.g. acetaminophen. Dispense no more than a 2-week supply.
	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.	

RECOMMENDED DRUG REGIMENS FOR TREATMENT OF LTBI IN PREGNANCY/POSTPARTUM

MONITORING OF PATIENTS ON TREATMENT FOR LTBI IN PREGNANCY/POSTPARTUM

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
- Provide counseling in patient's language to 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 baseline and monthly monitoring of liver function tests (LFTs) is indicated during treatment of LTBI in pregnancy and early postpartum.

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.

CANDIDATES FOR TREATMENT OF LTBI IN PREGNANCY/POSTPARTUM

CATEGORY OF WOMAN TESTED	TST <5 mm	TST ≥5 mm	TST ≥10 mm	TST ≥15 mm
HIV-infected and recent contact*	TREAT NOW	TREAT NOW	TREAT NOW	TREAT NOW
Immunosuppressed and recent contact*	TREAT NOW	TREAT NOW	TREAT NOW	TREAT NOW
HIV-infected*	Do Not Treat	TREAT NOW	TREAT NOW	TREAT NOW
Recent contact of TB case*	Do Not Treat	TREAT NOW	TREAT NOW	TREAT NOW
Resident/Employee institutional setting*§	Do Not Treat	Do Not Treat	TREAT NOW	TREAT NOW
Mycobacteria lab personnel*§	Do Not Treat	Do Not Treat	TREAT NOW	TREAT NOW

MAY DELAY TREATMENT UNTIL POSTPARTUM

Immunosuppressed persons	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
High-risk clinical conditions†	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

* Pregnant women with recent TB infection and/or HIV co-infection should be treated during pregnancy, even during first trimester. Contacts should receive a tuberculin skin test (TST) immediately and TST repeated 12 weeks after last exposure to TB case. Even if initial TST is 00 mm, an HIV-infected contact should continue treatment irrespective of results of TST at 12 weeks.

§ **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.



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TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI) IN PREGNANCY/POSTPARTUM

REVISED GUIDELINES FOR RIF-PZA

Target tuberculin skin testing (TST) for pregnant women only if at risk for TB:

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

Treat LTBI—it benefits the individual and the community.

Adherence is the key to successful prevention.

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