## RECOMMENDED DRUG REGIMENS FOR LTBI TREATMENT

Determine which regimen is most appropriate for your patient and support adherence to ensure successful completion. Evidence shows that patients are more likely to complete shorter regimens.

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<th>DRUG</th>
<th>INTERVAL AND DURATION</th>
<th>ADULT DOSAGE (MAX)</th>
<th>PEDIATRIC DOSAGE* (MAX)</th>
<th>COMPLETION CRITERIA</th>
<th>INDICATIONS</th>
<th>ADVERSE REACTIONS</th>
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<th>MONITORING FOR ALL PATIENTS</th>
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<tr>
<td><strong>INH</strong></td>
<td>Daily for 9 mos.</td>
<td>5 mg/kg (300 mg)</td>
<td>10–20 mg/kg (300 mg)</td>
<td>270 doses within 12 mos.</td>
<td>Recommended for most persons, and preferred for children &lt;12 years of age. Not indicated for persons exposed to INH-resistant TB.</td>
<td>Hepatitis risk increases with age, alcohol use, and concurrent use of other hepatotoxic drugs. Supplementation with pyridoxine (B6) should be considered in certain populations. See Managing Patients on Treatment.</td>
<td>• Evaluate at least monthly: Include careful questioning about adherence and side effects, and a brief physical examination. Check for evidence of hepatotoxicity, RPT hypersensitivity, or other adverse reactions: fever, anorexia, dark urine, icterus, rash, persistent paraphrenia of hands and feet, fatigue or weakness lasting 3 or more days, abdominal tenderness (especially in the right upper quadrant), easy bruising or bleeding, arthralgia, nausea, or vomiting.</td>
<td>• Baseline LFTs are indicated for: – 14V infection – Regular alcohol use – Pregnancy or &lt;3 months postpartum – History of liver disease or liver disorders – Risks for hepatic disease, including other potentially hepatotoxic drugs (e.g. anti-convulsants) or over-the-counter drugs (e.g. acetaminophen)</td>
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<td></td>
<td>Twice-weekly for 9 mos.</td>
<td>15mg/kg (900 mg)</td>
<td>20–40 mg/kg (900 mg)</td>
<td>76 doses within 12 mos.</td>
<td>DOT must be used with twice-weekly dosing</td>
<td>DOT must be used with twice-weekly dosing</td>
<td>• If side effects occur, a prompt physician’s evaluation is necessary with treatment changes as indicated.</td>
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<td><strong>INH</strong> and <strong>RIF</strong></td>
<td>Once-weekly for 12 weeks</td>
<td>Adults and children &lt;12 years of age: INH 15 mg/kg (900 mg max)</td>
<td>RIF 10.0–14.0 mg/kg (300 mg) 14.1–25.0 mg/kg (450 mg) 25.1–32.0 mg/kg (600 mg) 32.1–49.9 mg/kg (750 mg) &gt;50.0 mg/kg (900 mg max)</td>
<td>12 doses within 16 weeks</td>
<td>Recommended for otherwise healthy persons 12 years of age and older who were recently in contact with infectious TB or who recently converted their TB test from negative to positive or who have radiographic evidence of healed pulmonary TB. May be used in otherwise healthy HIV+ persons 12 years of age who are not on antiretroviral medications. May be considered for children 2–11 years of age if completion of 9 mos. INH is unlikely and hazard of TB is great. Not recommended for: • Children &lt;2 years of age • People with HIV/AIDS who are taking antiretroviral treatment • People presumed to be infected with INH or rifampin-resistant M. tuberculosis. • Pregnant women or women expecting to be pregnant while taking this regimen.</td>
<td>INH: as above RIF: Hematologic toxicity, hypersensitivity reaction (e.g. hypotension or thrombocytopenia), GI symptoms, polyarthralgia, hepatotoxicity, pseudo jaundice, flu-like symptoms, orange discoloration of bodily fluids.</td>
<td>• Hepatitis risk increases with age, alcohol use, and concurrent use of other hepatotoxic drugs. Supplementation with pyridoxine (B6) should be considered in certain populations. See Managing Patients on Treatment. Vigilance for drug hypersensitivity reactions, ranging from mild reactions such as Stevens-Johnson syndrome to more severe reactions including hypotension and thrombocytopenia. Consider possible rifamycin-associated drug interactions. See Managing Patients on Treatment. Women who use any form of hormonal birth control should be advised to also use a barrier method. Educate patients that orange discoloration of bodily fluids is expected and harmless. Consider possible rifamycin-associated drug interactions. See Managing Patients on Treatment. Women who use any form of hormonal birth control should be advised to also use a barrier method. Educate patients that orange discoloration of bodily fluids is expected and harmless.</td>
<td>Medication should be withheld and patients evaluated if: • Transaminase levels &gt;3 times upper limit of normal in presence of symptoms • Transaminase levels &gt;5 times upper limit of normal in asymptomatic patient • If children taking LTBI treatment develop hepatitis, discontinue treatment and seek other causes, noting transaminase levels stated above. • When LFTs have returned to normal, consider an alternate regimen, with close clinical and laboratory monitoring. Consult TB expert.</td>
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<td><strong>RIF</strong></td>
<td>Daily for 4 mos.</td>
<td>RIF 10 mg/kg (600 mg)</td>
<td>10–20 mg/kg (600 mg)</td>
<td>120 doses within 6 mos.</td>
<td>For contacts of patients with INH-resistant, RIF-susceptible TB, persons at risk or with serious adverse reactions from INH, or when short course treatment is preferred. In HIV-infected persons certain antiretroviral medications should not be given concurrently with RIF. An alternative with protease inhibitors is 150 mg of rifabutin daily. See <a href="http://www.aidsinfo.nih.gov">www.aidsinfo.nih.gov</a> for current guidelines.</td>
<td>GI intolerance, drug interactions, hepatitis, bleeding problems (from gums or other sites, easy bruising), flu-like symptoms, orange discoloration of bodily fluids.</td>
<td>Consider possible rifamycin-associated drug interactions. See Managing Patients on Treatment. Women who use any form of hormonal birth control should be advised to also use a barrier method. Educate patients that orange discoloration of bodily fluids is expected and harmless.</td>
<td>Report adverse events to CDC Division of Tuberculosis Elimination by sending an email to <a href="mailto:ltbidrugevents@cdc.gov">ltbidrugevents@cdc.gov</a></td>
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**Abbreviations:** INH = isoniazid, RIF = rifampin, RPT = rifapentine, NRTIs = nucleoside reverse transcriptase inhibitors, NNRTIs = non-nucleoside reverse transcriptase inhibitors, LFT = liver function test, DOT = directly observed therapy, mos. = months

* An additional regimen, 3 months of daily INH and RIF is included in the AAP Red Book as a possible alternative regimen, but is not currently included in CDC recommendations.

† Breastfeeding is not contraindicated in women taking INH. The amount of INH in breast milk is inadequate for treatment of infants with INH. Supplementation with pyridoxine (B6) is recommended for nursing women and for breastfed infants.

§ AAP recommends 10–15 mg/kg.

‡ AAP recommends 20–30 mg/kg.

§§ MDR-TB exposure: Consult TB expert. Decision to treat must consider likelihood of recent infection with MDR-TB strain, likelihood of developing TB disease, host factors, effective alternative regimen, monitoring, and follow-up.
For any regimen, support adherence to ensure successful completion by:

- Educate patients and caregivers about the importance of good adherence when treatment is initiated and throughout.

Pyridoxine (B6) supplements are recommended for persons taking INH who are pregnant and breastfeeding women.

Consider possible significant rifamycin-associated drug interactions including, but not limited to, hormonal contraceptives, antiretrovirals, methadone, oral hypoglycemics, anticoagulants, and psychotropic medications.

Rule out TB disease with an initial clinical examination, including symptom screen (for cough, fever, night sweats, alcohol use, HIV). Give pyridoxine 10-50 mg/day. Pyridoxine supplements are not required for RIF-only regimen.

Advise to stop treatment and promptly seek medical evaluation if these occur. Have clients explain what they understand back to you. Use a trained interpreter if language is a barrier.

For any regimen, support adherence to ensure successful completion by:

- Identifying possible barriers to adherence (appointment conflicts, misinformation about TB, health beliefs and practices, limited financial resources, co-existing medical conditions, medication side effects, language barriers, real or perceived stigma)
- Collaborating with community agencies to obtain incentives and/or enablers, case management or directly observed therapy
- Providing effective patient education and patient-focused strategies