

Intermittent Short Course Treatment Regimen for Tuberculosis Infection

The Centers for Disease Control and Prevention (CDC) recommends the combination of isoniazid (INH) and rifapentine (RPT) given as 12 weekly doses, using directly observed therapy (DOT), as an alternative to 9 months of daily, self-administered INH for treating latent TB infection (LTBI) in several high-risk patient groups.¹ This recommendation was made following publication of a study completed by the CDC TB Trials Consortium.²

CDC Guidelines

You may consider the 12-dose regimen for healthy patients aged ≥ 12 (twelve) years who have one of the following predictive factors for greater likelihood of developing TB:

- **Latent TB infection thought to be due to recent exposure to contagious TB (*i.e.*, infected contacts)**
- **Conversion from negative to positive test for latent TB infection (as defined by CDC Guidelines for tuberculin skin test conversion³ and for an interferon-gamma release assay as negative-to-positive)**
- **Radiographic findings of healed pulmonary TB, once active tuberculosis has been ruled out**
- **Healthy HIV-infected patients who are not taking antiretroviral medications**

NOTE: The 12-dose regimen is specifically is **NOT RECOMMENDED** for:

- Children < 2 (two) years of age
- HIV-infected persons on antiretroviral therapy
- Presumed infection with INH- or rifampin-resistant TB, or
- Pregnant women

| Once-weekly oral regimen | | |
|--|------|--|
| <i>All doses administered under direct observation (DOT) by a trained worker</i> | | |
| Isoniazid | PLUS | Rifapentine |
| 15 mg/kg rounded up to the nearest 50 or 100 mg (900 mg max) | | 10.0–14.0 kg: 300 mg 14.1–25.0 kg: 450 mg 25.1–32.0 kg: 600 mg 32.1–49.9 kg: 750 mg ≥ 50.0 kg: 900 mg maximum |

While some experts suggest this regimen may be used in other situations, based on currently available published data, the Massachusetts TB Program does not recommend routine use of the 12-dose INH+RPT regimen outside the four groups described above, *i.e.*, contacts, converters, old TB on X-ray, or HIV-infected not taking antiretrovirals. This regimen has not been studied in populations of children under 12 years of age.

¹ CDC. Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent *Mycobacterium tuberculosis* infection. MMWR 2011;60:1650-1653. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm>

² Sterling TR, *et al.* Three months of once-weekly rifapentine and isoniazid for *M. tuberculosis* infection. N Engl J Med 2011; 365: 2155–66. <http://www.ncbi.nlm.nih.gov/pubmed/22150035>

Monitoring

- Because missed doses, or altered dosing intervals or amounts, could jeopardize efficacy or safety, the INH+RPT regimen should be administered by DOT; this can be done at the provider's office or at a location chosen for mutual convenience (*e.g.* home or school clinic).
 - At each encounter, patients should be instructed to seek immediate medical attention if they have fever, yellow eyes, dizziness, syncope, rash, aches; or nausea, vomiting, weakness, abdominal pain, or loss of appetite.
 - INH+RPT should be withheld while the cause of symptoms is being determined.
- Patients should undergo a clinical assessment at least monthly, to include inquiries about side effects and a physical examination.
 - Blood tests (CBC and hepatic enzymes) generally are not recommended for everyone, but baseline and subsequent tests should be performed for certain patients at higher risk for toxicity.³

Special precautions

- Active TB must be ruled out before treatment for latent TB infection is considered.³
- *Rifapentine, like rifampin, affects the metabolism of many drugs*, such as hormonal contraceptives, antidepressants, oral anticonvulsants, antiarrhythmic drugs, oral anticoagulants, methadone, and others. Appropriate adjustments must be made if treatment with RPT is being considered.
- Cost and drug availability: Programmatic costs of drug (RPT), monitoring, and DOT must be considered before beginning a program utilizing this regimen.

ADVERSE EVENTS should be reported to FDA via MedWatch:
<https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>

Report TB:

Report newly diagnosed cases of latent TB infection, and suspected or confirmed TB disease to the Massachusetts Department of Public Health.

<http://www.mass.gov/eohhs/gov/departments/dph/programs/id/isis/case-report-forms.html>

For more information, contact the MDPH TB Program: 617-983-6970

www.mass.gov/dph/cdc/tb

³ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6).
<http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>