Use of a Weekly Regimen of 12 Doses of Isoniazid and Rifapentine for the Treatment of Latent Tuberculosis Infection
Recommendations of the Connecticut Advisory Committee for the Elimination of Tuberculosis

In December 2011, the Centers for Disease Control and Prevention (CDC) released recommendations on a new option for the treatment of latent tuberculosis infection (LTBI) (1). The new option uses a weekly regimen of 12-doses of isoniazid (INH) and rifapentine (RPT) **given by** directly observed therapy (DOT). This recommendation was made after publication of a large randomized controlled trial and review of two other studies that showed this regimen to be as effective for preventing TB as the standard 9 month regimen using INH alone and is more likely to be completed. This new regimen with fewer doses is one of the biggest advances in LTBI treatment in 40 years.

This document is meant to summarize the recommendations published by CDC and give guidance on the use and implementation of this new regimen in Connecticut. The CDC recommendations can be found at http://www.cdc.gov/mmwr/pdf/wk/mm6048.pdf and should be reviewed by all clinicians intending to prescribe this regimen to their patients.

It should be noted that this regimen is meant to serve as an additional option for LTBI treatment but does not replace other recommended regimens including INH daily for 9 months.

Recommended Patient Populations

INH-RPT is recommended for healthy patients ≥12 years old with LTBI who also have at least one risk factor for progression to TB disease; this includes recent known contacts to a person with infectious TB, conversion from negative to positive on a tuberculin skin test or interferon gamma release assay, radiographic findings of healed pulmonary TB (after active TB has been ruled out with AFB smear and culture) and HIV-infected patients who are not on anti-retroviral treatment. This regimen can be considered on a case-by-case basis for other types of patients. The preferred regimen for children 2–11 years old remains INH daily for 9 months as the studies reviewed did not have enough children in this age group to assess efficacy and tolerability. However, 12 weekly doses of INH-RPT can also be considered for children on an individual basis if the child is at high risk for development of TB disease and it is unlikely they could complete 9 months of INH therapy.

This regimen is not recommended for children <2 years old, HIV-positive patients taking antiretroviral treatment, pregnant women and patients who have been exposed to TB resistant to either INH or rifampin.

Dosing and Administration

Dosing instructions for INH and RPT as part of this regimen are outlined below, based on the weight of the patient. Most adult patients (≥50 kg or 110 lbs) will be on the maximum dose of both medications. Adverse effects of both medications and interactions with other medications should be reviewed with all patients. Given the interaction of RPT with hormonal contraceptives, women taking these medications should be advised to switch to or add a barrier method to prevent pregnancy.

INH- 15 mg/kg rounded up to the nearest 50 or 100 mg, 900 mg maximum dose

RPT-	10–14 kg	300 mg
	14.1–25 kg	450 mg
	25.1–32 kg	600 mg
	32.1–49.9 kg	750 mg
	≥50 kg	900 mg (maximum dose)

It is not entirely clear what minimum number of doses of this regimen is adequate for LTBI treatment. In the randomized clinical trial of this regimen, a patient was considered to have completed treatment if they took at least 11 doses within 16 weeks with all doses separated by at least 72 hours (2).

Since this regimen is dosed on a weekly basis and missed doses could jeopardize efficacy and/or safety, **ALL** doses should be administered and documented using DOT by a trained health worker to ensure patient compliance and tolerance. The weekly visit should also be used to review potential side effects and reinforce the importance of continuing and completing therapy. DOT can be performed in a variety of ways. For most patients, the easiest scenario will likely be to present to the clinic or physician's office at a predetermined time each week. Other patients might need a nurse to come to their home. For children, DOT can often be set-up through a school-based health clinic. The local health department or the DPH TB Control Program can be contacted to help determine resources for DOT for patients before starting this regimen. Please call the 860-509-7722 with questions regarding reimbursement for DOT by the DPH TB Control Program.

Clinical Monitoring

As with any patient on LTBI therapy, it is recommended that patients be seen at least monthly to undergo a physical exam and assessment for adverse drug effects. Baseline hepatic chemistry tests are not recommended for all patients but should be done for the following patient groups: HIV infection, liver disorders, postpartum women (≤3 months after delivery), and regular alcohol usage. Baseline liver tests should be considered for older patients (age ≥60 years), especially those with chronic medical conditions. Subsequent blood tests should be done when baseline tests are abnormal, for those at risk for liver disease, and if symptoms concerning for adverse drug effects develop.

All adverse drug effects resulting from this regimen should be immediately reported to the DPH TB Control Program (860-509-7722) so that they can be forwarded to the CDC and Food and Drug Administration (FDA).

Requesting Medication from the DPH TB Control Program

Since this is a new regimen, it is recommended that all patients prescribed INH-RPT receive their medications from the DPH TB Control Program. All medication for the full course of treatment will be provided free of charge, regardless of insurance status of the patient.

To obtain medication for a patient, the Latent Infection Surveillance Report Form (available at http://www.ct.gov/dph/lib/dph/infectious_diseases/tb/pdf/tb_latent_infection_entry_form.pdf) should be completed and faxed to the TB Control Program (860-509-7743) with a prescription for both the INH and RPT. **On the prescription, the clinic or person performing DOT should be documented. Prescriptions will not be filled without documentation of the DOT provider.** The full three months of medication will be mailed to the requesting healthcare provider who should retain all medications at their office rather than distributing them to the patient unless the patient is receiving DOT in their home.

At each monthly visit and at the end of treatment, it is requested that the clinician fill out the Tuberculosis Therapy and Follow-Up Care Report Form (TB-32 form) (available at http://www.ct.gov/dph/lib/dph/infectious_diseases/tb/pdf/tb32_entry_form.pdf) and fax or mail to the TB Control Program. This ensures documentation of continued therapy and completion of treatment in our database.

Please call the TB Control Program at 860-509-7722 with any questions or concerns about this new option for LTBI treatment.

References

1. CDC. Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent *Mycobacterium tuberculosis* infection. MMWR 2011; 60: 1650–53.

2. Sterling TR, Villarino ME, Borisov AS, et al. Three months of once-weekly rifapentine and isoniazid for *M. tuberculosis* infection. N Engl J Med 2011;365:2155–66.