Recommendations for the Use of the 12-week Isoniazid and Rifapentine Regimen for the Treatment of Latent Tuberculosis Infection

Treatment for latent tuberculosis (TB) infection (LTBI) can prevent progression to active TB disease. Isoniazid (INH) once daily for 9 months is currently the preferred treatment regimen for most individuals with LTBI. In December 2011, the Centers for Disease Control and Prevention (CDC) issued recommendations in which isoniazid and rifapentine (INH-RPT) once-weekly for 12 weeks administered by Directly Observed Therapy (DOT) is considered an equal alternative to the 9-month INH regimen for some individuals. INH-RPT reduces the length of treatment from 270 daily doses given over 9 months to 12 once-weekly doses given over 12 weeks. The Minnesota Department of Health (MDH) recommends that the following factors be addressed when considering the use of INH-RPT for the treatment of LTBI:

1. INH-RPT does not replace other recommended LTBI treatment regimens; it is another effective regimen option for otherwise healthy patients aged ≥12 years who have at least one predictive risk factor for developing active TB disease including:
   a. recent exposure to contagious TB
   b. conversion from negative to positive tuberculin skin test (TST) or Interferon Gamma Release Assay (IGRA) within previous 2 years
   c. radiographic findings of inactive, “healed” pulmonary TB
   d. HIV/AIDS but not taking antiretroviral medications
   e. medical or social circumstances that make adherence and completion of longer regimens unlikely

2. INH-RPT is not recommended for:
   a. Children younger than 2 years of age
   b. Patients with HIV/AIDS who are taking antiretroviral treatment
   c. Patients with presumed INH or rifampin-resistant LTBI
   d. Pregnant women or women expecting to become pregnant during treatment

3. The preferred regimen for children aged 2-11 years is 9 months of daily INH. However, INH-RPT can be considered on a case-by-case basis.

4. DOT is mandatory. Studies supporting the efficacy and tolerability of INH-RPT were based on treatment protocols using DOT provided by public health agencies. Therefore, MDH strongly recommends the use of DOT by local health department staff for INH-RPT patients. Individual local health departments should determine whether to provide DOT for INH-RPT. Decisions should be based on the patient’s risk of developing active TB, available local resources for providing DOT, the capacity for monthly patient monitoring, and the patient’s likelihood of successfully completing treatment.
5. MDH will provide INH-RPT free-of-charge on a case-by-case basis for patients who meet the CDC-recommended eligibility criteria AND for whom a specific plan is in place to provide the recommended monthly physical examinations and DOT. MDH strongly recommends against the self-administration of INH-RPT. Requests for INH-RPT medication from MDH should be accompanied by a completed INH-RPT Checklist form in addition to the Request for Medication to Treat Latent TB Infection (LTBI) form for each individual.

6. For INH-RPT, INH is dosed at 15mg/kg; round up to the nearest 50 or 100 mg to a maximum dose of 900 mg. RPT is dosed at 150-mg increments, adjusted for weight, with a minimum dose of 300 mg and a maximum dose of 900 mg. RPT is packaged in blister packs that should be kept sealed until used.

7. Doses should ideally be spaced 7 days apart. At a minimum, 72 hours must elapse between doses. The minimum amount of time required for the regimen is 12 weeks and the maximum is 16 weeks. **INH-RPT cannot be administered in less than 12 weeks.** Missed doses or altered dosing intervals or amounts could jeopardize efficacy or safety of this regimen.

8. Patients should have a pre-treatment clinical evaluation to rule out active TB disease and to assess for the likelihood of adverse effects of therapy. Prior to starting treatment, pregnancy should be ruled out in females, and the patient should agree to not become pregnant during treatment. If pregnancy occurs, INH-RPT should be discontinued.

9. Patients should be educated about what is expected of them for the INH-RPT regimen. They should agree to take up to 10 tablets at each DOT visit, to be available for DOT as scheduled, to commit to 12 weeks of treatment and monthly physical examinations. If these cannot reasonably be assured, one of the other LTBI treatment regimens should be used.

10. Obtain a list of the patient’s current medications and consider potential drug interactions. Some interactions to note:
   a. INH increases blood levels of phenytoin (Dilantin) and disulfiram (Antabuse)
   b. RPT decreases blood levels of many drugs including oral contraceptives, warfarin, sulfonureas, and methadone
   c. RPT is contraindicated in HIV-infected individuals being treated with protease inhibitors (PIs) and most nonnucleoside reverse transcriptase inhibitors.

11. Advise patients taking RPT that they will notice a normal orange discoloration of body fluids, including urine and tears. Contact lenses may be permanently stained. In addition, RPT decreases the efficacy of hormonal birth control; women who use any form of hormonal birth control should be advised to add, or switch to, a barrier method.

12. Baseline and follow-up laboratory monitoring during treatment of LTBI are not routinely recommended by CDC but should be provided for certain high-risk patients. See CDC recommendations for additional information.

13. Patients taking INH-RPT should be assessed at weekly DOT visits for evidence of hepatitis or other adverse effects, and for symptoms of active TB disease. At each visit, patients should be instructed to seek medical attention immediately if they have: fever, yellow eyes, dizziness, rash, or aches or >1 day of nausea, vomiting, weakness, abdominal pain, or loss of appetite. INH-RPT should be withheld while the cause of symptoms is being evaluated.
14. In addition to weekly DOT visits, patients receiving the INH-RPT regimen need a monthly physical
exam to assess for the presence of jaundice, liver tenderness, and rash.

15. According to CDC, INH-RPT was well tolerated in treatment trials. However, with previous LTBI
regimens (e.g., INH, rifampin-pyrazinamide), fatal liver injuries came to attention only after the
regimens were widely adopted. Adverse events leading to hospitalization or death associated with the
use of any LTBI regimen should be reported to MDH (651-201-5414) for inclusion in CDC’s adverse
events surveillance system, and to FDA MedWatch at http://www.fda.gov/medwatch.

Adapted by the Minnesota Department of Health from:

Centers for Disease Control and Prevention. Recommendations for the Use of an Isoniazid-Rifapentine Regimen with Direct

Frequently Asked Questions, Heartland National TB Center on the INH-RPT regimen. TBeat newsletter March 2012, Volume