

A. Background

1. On December 9, 2011, The Centers for Disease Control and Prevention published the following article in the Morbidity and Mortality Weekly Report, Vol. 60, No. 48, pp. 1650-1653: “Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection”.
2. DSHS has implemented the use of Isoniazid-Rifapentine (INH-RPT) for LTBI, using once-weekly directly observed therapy for 12 weeks as **the preferred regimen for treating LTBI in persons 12 years of age and older, unless contraindicated by CDC guidelines**”.
3. Perform all relevant activities and follow all applicable recommendations within **ATTACHMENT #2: Nursing Management of Clients Infected with TB (LTBI) or Clients Requiring Window Prophylaxis**

B. Clients for whom INH-RPT is recommended

1. Contacts age 12 and older with LTBI, otherwise healthy, who have a predictive factor for greater likelihood of TB developing, including:
 - Recent exposure to contagious TB
 - Positive IGRA or TST result - Recommendation from the Texas TB Expert Panel: Use of IGRA as the preferred testing regimen will decrease the number of false positives, allowing for an appropriate focus of resources.
 - Radiographic findings of healed pulmonary TB after a diagnosis of TB disease has been definitively ruled out (see ATTACHMENT #2: Nursing Management of Clients Infected with TB (LTBI) or Clients Requiring Window Prophylaxis).
2. LTBI in otherwise healthy adult clients with a predictive factor for greater likelihood of developing TB and unlikely to complete 9 months of daily INH therapy.
3. Adult clients diagnosed with LTBI who have HIV infection, are otherwise healthy, and not on anti-retroviral therapy. Antiretroviral therapy should not be delayed to give INH-RPT. If antiretroviral therapy is to be started, give an alternative LTBI regimen such as INH for 9 months. Obtain a consult with a physician who is knowledgeable about both HIV and TB regarding which therapy to provide: antiretroviral therapy or INH-RPT.
4. High priority groups (age 12 and older) with LTBI in situations where INH-RPT offers practical advantages:
 - Homeless clients.

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ATTACHMENT #3: Nursing Management of Clients Treated for LTBI with Isoniazid-Rifapentine (INH-RPT) by DOT Once Weekly for 12 Weeks

- Students 12 years of age and older who have been exposed to infectious TB disease and could receive directly observed therapy from a school nurse.
 - Contacts in the household of a case already receiving DOT.
 - Highly mobile clients such as truckers or pilots.
5. Clients 2-11 years of age can be considered on a case-by-case basis when both 1. the circumstances make the completion of 9 months of daily INH unlikely and 2. the likelihood or the hazard of TB is great (e.g., recent TB infection in a preschool aged child). The number of children in this age range who have received INH-RPT is insufficient for assessing tolerability and efficacy. Obtain a consultation from a DSHS-recognized expert TB physician before using.

C. INH-RPT is not recommended for the following:

1. Clients under 2 years of age.
2. Clients with HIV infection who are receiving antiretroviral therapy.
3. Clients who are pregnant or expecting to become pregnant during the 12 weeks of therapy.
4. Contacts to cases who are resistant to INH and/or the rifamycins (rifampin, rifapentine, rifabutin).
5. TB suspects or cases.
6. Allergy to the rifamycins or INH.
7. HIV infected clients with respiratory symptoms who are being considered for treatment of LTBI, even if the CXR is normal. If results of sputum smears and cultures are negative and respiratory symptoms can be explained by another etiology, then a regimen with INH-RPT can be started, if the patient is not taking antiretroviral medications. If bacteriologic results are negative but the activity or etiology of a radiographic abnormality is questionable, further evaluation should be undertaken. Treatment of LTBI should not be started until active TB has been excluded.

D. Rifapentine has many drug-drug interactions and a pharmacologic reference must be consulted to ensure the client is not on a medication that, when taken with RPT, is contraindicated, recommended to avoid, requires monitoring or modification of treatment, or caution is advised. If the client is on a medication that could potentially interfere with RPT, do not start INH-RPT and consult the authorizing physician.

- E. **Rifapentine is a category C drug**, in which animal studies have shown adverse fetal effects but no controlled human studies performed OR no animal or human studies performed. **Because safety in pregnancy is unknown**, additional considerations for female clients of childbearing potential include, but are not limited to:
1. For female clients of childbearing potential: counsel the client that rifamycins may make hormonal contraceptive methods less effective, encourage the client to add a back-up barrier method to prevent pregnancy, and emphasize the importance of avoiding pregnancy while on treatment.
 2. Document the birth control methodology and the date of the last menstrual period for all women of child bearing potential.
 3. Document whether the client thinks she may be pregnant. If the client becomes pregnant or suspects she may be pregnant during treatment with INH-RPT, discontinue this regimen and consult with the authorizing physician as to which alternative treatment regimen to give.
 4. If pregnancy is suspected prior to initiation of treatment, do not start INH-RPT until pregnancy is excluded.
 5. If avoidance of pregnancy cannot be assured for any woman of childbearing potential, consider using an alternate LTBI regimen.
 6. Have the client sign the Disclosure and Consent Form for Drug Therapy for Treatment of Latent Tuberculosis (TB) Infection: INH and Rifapentine treatment **TB -415B**.
- F. **Treatment with INH-RPT is by DOT only**
1. Each medicine dosage is calculated by body weight:

BOX 1. Dosage for a combination regimen of isoniazid and rifapentine in 12 once-weekly doses under direct observation for treating latent *Mycobacterium tuberculosis* infection.

Isoniazid

15 mg/kg rounded up to the nearest 50 or 100 mg;
900 mg maximum

Rifapentine

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

Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifapentine (RPT) is formulated as 150 mg tablets packed in blister packs that should be kept sealed until usage. New formulations with larger dosage per tablet and fixed-dose INH-RPT combinations are in development.

Source: Three months of weekly rifapentine and isoniazid for *Mycobacterium tuberculosis* infection (PREVENT TB). Information available at <http://clinicaltrials.gov/ct2/show/nct00023452?term=rifapentine&rank=9>.

Source: Recommendations for use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. MMWR Dec 9, 2011. 60(48); 1651-1653.

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm>

2. Provide the correct number of INH and RPT tablets to the client and observe the client take each weekly dose. Be sure to ask all of the toxicity questions on form **TB-206A** prior to the patient swallowing each dose.
3. Counsel the client on side effects and symptoms of side effects, especially hypersensitivity reactions and drug induced liver injury.

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4. Hypersensitivity reaction: fever, headache, dizziness, musculoskeletal pain, petechiae, purpura, pruritis, hypotension.
5. Drug induced liver injury (hepatitis): fever, yellow eyes and/or skin, dizziness, aches, or greater than 1 day of nausea, vomiting, weakness, abdominal pain, loss of appetite.
6. Completion of treatment is defined as 11 or 12 doses taken in 16 weeks. Each dose must be separated by at least 72 hours. Only in extreme circumstances should this period be reduced to less than weekly dosing; for example, to prevent a patient from missing a dose. **Consult with the authorizing physician if a dose is anticipated to be given early.** Do not shorten the dosing interval on a routine basis.
7. Discontinue INH-RPT if aminotransferase concentration exceeds more than 5 times the upper limit of normal (with or without symptoms) or more than 3 times normal in the presence of symptoms. Evaluate the patient carefully and consult the treating physician. Do not restart the regimen without obtaining a new order from the authorizing physician.

G. References

- 1) Jereb, J. A., et al. "Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection". MMWR December 9, 2011, 60:48, 1650-1653.
- 2) DSHS TB Expert Physicians' Conference Call, December 16, 2011.
- 3) Pugh, Maureen Barlow (Ed., et al). Stedman's Medical Dictionary, 27th Edition. Philadelphia: Lippincott, Williams & Wilkins, 2000.
- 4) Centers for Disease Control and Prevention, "Fact Sheet: Treatment Options for Latent Tuberculosis Infection." Available at:
http://www.cdc.gov/tb/publications/factsheets/treatment/LTBI_treatment_options.htm
- 5) Nursing 2012 Drug Handbook, 32nd edition. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2012.