

UTAH DEPARTMENT OF HEALTH (UDOH) GUIDANCE FOR THE MANAGEMENT OF PERSONS ON TREATMENT FOR LATENT TUBERCULOSIS (TB) INFECTION (LTBI) WITH ISONIAZID (INH) AND RIFAPENTINE (RPT), ALSO KNOWN AS 3HP BY DOT OR SELF-ADMINISTERED THERAPY (SAT), WEEKLY FOR 12 WEEKS

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. On October 1, 2012 our state TB physician consultants recommended, with caution, the implementation of the CDC use of the INH-RPT regimen for LTBI, using directly observed therapy (DOT) for 12 weeks.
3. On June 29, 2018, CDC revised their recommendations to: 1) lower the acceptable age to ≥ 2 , 2) recommend 3HP for persons with HIV/AIDS being treated with antiretrovirals having acceptable drug-drug interactions with rifapentine (see CDC Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents) , and 3) recommend dosing by either DOT or SAT.
4. UDOH recommends the use of the 12 weeks directly observed therapy INH-RPT regimen for LTBI for persons age 2 or older who meet the following criteria:
 - A. Contacts with LTBI, with recent exposure to sputum smear positive TB.
 - B. Documented conversions of Tuberculin Skin Test (TST) or Interferon-Gamma Release Assay (IGRA).
 - C. Individuals with a predictive factor for greater likelihood of developing TB and risk factors for not completing 9 months of INH therapy.
 - D. Radiographic findings of healed pulmonary TB after a diagnosis of TB disease has been definitively ruled out.
 - E. Persons diagnosed with LTBI who are HIV +, otherwise healthy, and not on anti-retroviral therapy that have unacceptable drug-drug interactions with rifapentine.
5. Treatment using state-funded medication may be used for the following high-priority groups (if insured, UDOH will determine whether to use state drugs, or reimburse the pharmacy for the copay):
 - A. Exposed contacts to a sputum smear positive case;
 - B. Newly arrived refugees;
 - C. HIV+ individuals;
 - D. Patients on high-dose steroids, TNF alpha antagonists; those awaiting a transplant, dialysis patients, diabetics, and others on a case-by-case basis.
5. **This drug regimen is contraindicated for and is not recommended for the following persons:**
 - A. Children under 2 years of age.
 - B. Women who are pregnant or likely to become pregnant during the 12 weeks of therapy and those who are sexually active and do not agree to use a barrier method of contraception in place of/addition to hormonal agents.
 - C. Contacts to cases who are resistant to INH and/or the rifamycins (rifampin, rifapentine, rifabutin).
 - D. TB suspects or cases.

- F. Persons on medications which should only be used after consideration of the drug-drug interactions with rifampine, especially those drugs that follow the cytochrome p450 pathway, and for whom careful monitoring can be provided include:
 1. Warfarin sodium (Coumadin),
 2. Dilantin,
 3. Phenobarbital,
 4. Psychotropic drugs,
 5. Methadone,
 6. Disulfuram (Antabuse),
 7. Chemotherapy Agents,
 8. Hormonal birth control,
 9. Other drugs also known to carry the same warning with Rifampin.

- 6. Baseline assessment of clients for this regimen includes:
 - A. Health history, including medications (prescription and non-prescription medications and herbal supplements) the patient is taking, social history, medical history, TB history, and signs and symptoms of TB.
 - B. Temperature, weight and blood pressure at baseline.
 - C. Document date of last menstrual period for women of child bearing age
 1. If a woman is taking Depo-Provera injections for contraception, she may not have menstrual periods. Assess for date of last Depo-Provera injection.
 - D. Document the birth control methodology for all potentially sexually active females:
 1. If pregnancy is suspected, draw a serum pregnancy test and delay start of medication until a negative test result is received. If the serum pregnancy test result is positive, this patient cannot take the INH-RPT regimen; it is contraindicated in pregnancy.
 - E. Obtain liver function test (including AST, ALT and total bilirubin) and CBC with platelets with:
 1. HIV infection,
 2. Liver disorders, including hepatitis B and C, cirrhosis,
 3. In the immediate postpartum period (less than or equal to 3 months after delivery),
 4. Regular alcohol usage or alcohol abuse,
 5. Patients of any age taking medications that are potentially hepatotoxic,
 6. Persons with diabetes.
 7. Persons with blood dyscrasia-causing conditions.
 - F. Refer for medical evaluation if the baseline liver function tests and/or the CBC with platelets are elevated or the platelet level is less than 100,000.
 - G. If the baseline CBC with platelets and/or baseline liver function tests are abnormal, delay the start of treatment until authorized by the physician.
 - H. HIV test based on risk assessment.
 - I. A woman who is within the three month post-partum period must have careful laboratory and clinical monitoring. Draw liver function tests and a CBC with

platelets at baseline and every month during treatment. Ensure the clinical monitoring listed in section 8 of this standing delegation order is done with every dose and monthly.

7. Treatment is by DOT or SAT. A gift certificate incentive in the amount of \$10 may be offered for every dose the patient receives *at your facility*. Video DOT (VOT), also known as eDOT may be used at the discretion of the local health department. Please see UDOH policy and protocol for VOT, and maintain required documentation (access via UDOH TB website, Information for Health Care Providers and Public Health, TB Resources, Treatment)

A. Each medicine dosage is calculated by body weight:

Isoniazid

15 mg/kg rounded up to 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 kg or greater = 900 mg maximum

Isoniazid is formulated as 100 mg and 300 mg tablets. Rifapentine 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.

- B. Review s/s medication side effects (see 8B) and s/s active TB before start of treatment and each dose, and complete DOT log (if dosing is SAT, have patient complete log and review with you monthly).. If any are reported, notify PHN before dosing. (An RN or MD should review the above with the patient before initiating regimen.)
- C. Completion of treatment is defined as 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. Do not shorten the dosing interval on a routine basis.
- D. At the beginning of treatment, obtain enough medication for the entire 12 doses for each patient before starting treatment, to avoid treatment interruption due to drug supply problems.
- E. Give pyridoxine, based on weight (max 50 mg/week) to
1. Persons with diet deficient in vitamin B6
 2. Persons who abuse alcohol
 3. Patients with diabetes
- F. If diagnosed with LTBI and HIV at the same time, work with the HIV provider to make a decision as to regimen safety. Anti-retroviral therapy should not be delayed to give INH and RPT. If incompatible anti-retroviral therapy is to begin, give another LTBI treatment regimen that does not conflict with the anti-retroviral

therapy. Get an expert medical consultation if needed to determine which therapeutic regimen to give with anti-retroviral therapy.

- G. The assessment and initial dose of INH and RPT is to be given by a registered nurse.

8. Monitoring

- A. If dosing is by DOT, at every DOT visit ask all questions on the DOT Log. If the patient answers yes to any symptom, the DOT worker must call the TB nurse for instructions about whether to give the medication. If SAT, instruct patient to complete log each week and report any side effects (such as: fever, yellow eyes or skin, dark urine, light-colored stool, dizziness, rash, aches, bleeding gums, easy bruising, mouth sores, nausea, vomiting, diarrhea, weakness, abdominal pain, or loss of appetite) immediately. 3HP should be withheld until deemed safe by the PHN, in consult with MD.
- B. At least monthly, patients should undergo a clinical assessment, including inquiries about side effects and s/s active TB and a targeted physical examination (see C below). Any abnormalities should be discussed with state (or your) physician consultant. Meds should be stopped pending physician consult.
- C. The physical examination should include vital signs (temperature, weight and blood pressure), inspection of the skin and eyes for jaundice and the mouth for lesions, assessment for rash, and inquiries regarding fatigue, GI upset, urine or stool discoloration.
- D. Subsequent liver function tests (including ALT, AST and total bilirubin) and/or CBC with platelets should be drawn monthly for:
 1. Patients whose baseline or subsequent testing is abnormal.
 2. Patients at risk for/hx of liver disease.
 3. Hx blood dyscrasias.
 4. HIV infection.
 5. Patients within the three month postpartum period.
 6. Regular alcohol use or alcohol abuse.
- E. Discontinue INH-RPT if a serum aminotransferase concentration is greater than or equal to five times the upper limit of normal even in the absence of symptoms or greater than or equal to three times the upper limit of normal in the presence of symptoms. Refer for medical care and consult the physician for the patient's plan of care. **Do not restart the regimen without a new physician's order.**
- F. Document the date of a woman's last menstrual period monthly at the clinical assessment visit. If the patient becomes pregnant during treatment with INH-RPT, discontinue this regimen. Remember, if a woman is taking Depo-Provera injections for contraception, she may not have menstrual periods. Assess the date of last Depo-Provera injection and the date that the next injection is scheduled. If a woman's menstrual period is >3 days late, hold the INH and RPT and check a serum pregnancy test. Do not restart medications unless the pregnancy test is negative.
- G. Report severe adverse drug effects to UDOH TB Nurse Consultant, 801-538-9906.

1. Adverse reactions resulting in hospitalization or death should be reported to the CDC Division of Tuberculosis Elimination at 404-639-8401 or LTBIdrugevents@cdc.gov
2. Adverse events or medication errors also should be reported to FDA MedWatch at <http://www.fda.gov/medwatch>, by submitting a MedWatch Form 3500 (available at http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf) or by calling 1-800-FDA-1088.

References

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