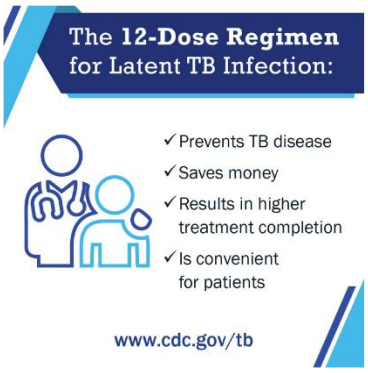
Updated Recommendations for Use of Isoniazid and Rifapentine (3HP) to Treat LTBI



The CDC recently announced updated recommendations for the use of 3HP to treat LTBI, and the full text of the CDC recommendations can be found in the June 29, 2018 issue of the Morbidity and Mortality Weekly Report (MMWR)[i]. The key updates address the use of 3HP in children and in patients with human immunodeficiency virus (HIV) infection (including acquired immunodeficiency syndrome, or AIDS) and introduce the opportunity for patients to self-administer 3HP.

Background

Treatment of LTBI is essential to control and eliminate TB in the United States because it substantially reduces the risk that latent TB infection will progress to TB disease.

Since the CDC first recommended 3HP for the treatment of LTBI in 2011, additional research has been done in multiple patient populations to evaluate the efficacy, safety and treatment completion rates for 3HP. In 2017, a CDC Work Group began a systematic review and meta-analysis of published data for the 3HP regimen. These results were published in June 2018[ii]. The meta-analysis determined that 3HP "is as safe and effective as other recommended [LTBI] regimens and achieves substantially higher treatment completion rates."

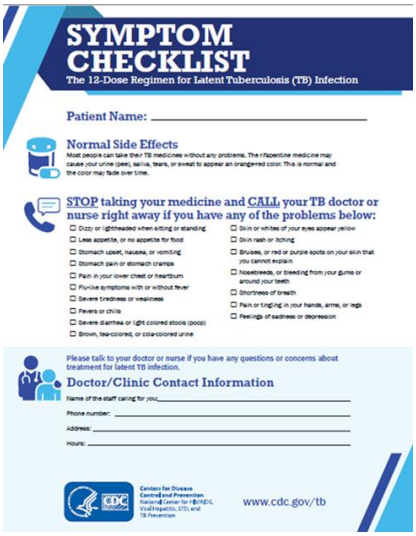
Based on the meta-analysis, the CDC continues to recommend 3HP for treatment of LTBI in adults and now recommends use of 3HP:

- In persons with LTBI aged 2 to 17 years;
- In persons with LTBI who have HIV infection, including AIDS, and are taking antiretroviral medications with acceptable drug to drug interactions with rifapentine; and
- By directly observed therapy (DOT) or self-administered therapy (SAT) in persons aged 2 years and older.

The CDC advises health care providers to choose the mode of administration (either DOT or SAT) based on local practice, individual patient attributes and preferences, and other considerations such as the patient's risk for progressing to severe forms of TB disease[iii].

The CDC recommends that all individuals on 3HP be evaluated monthly to assess compliance with treatment and side effects. It also recommends that patients taking 3HP via SAT be encouraged to maintain a medication diary in which they record each date they took their medication and any difference in the day of the week they took their medication (e.g., the patient agreed to take their medication every Tuesday but took it on Wednesday in week 4).

Copies of a Medication Tracker and Symptom Checklist can be found on the CDC's TB page.



Lastly, the updated CDC recommendations state that additional studies are needed to understand the:

- Pharmacokinetics, safety and tolerance of 3HP in children less than 2 years of age;
- Adherence to and safety of 3HP when self-administered by persons aged less than 18 years; and the
- Safety of 3HP during pregnancy.

Pennsylvania (PA) TB Program Recommendations

The PA TB Program encourages increased use of the 3HP regimen to treat LTBI in appropriate patients. After reviewing the updated CDC recommendations in consultation with the state TB medical consultants, the TB Program recommends adopting the CDC recommendations with the following exceptions:

- Patients 15 years of age and younger should receive 3HP via DOT. Self-administered therapy (SAT) with 3HP has not been studied in persons younger than 18 years of age.
- Strong consideration of the patient's age, medical history, social circumstances, and risk factors for progression to severe TB disease should be given when deciding how to administer 3HP.
  - DOT is strongly recommended for patients 16 years of age and older on 3HP at **high risk** of progression to TB including, but not limited to: persons with conditions such as end stage-renal disease, diabetes mellitus, and organ transplantation; persons who use alcohol or illegal drugs; and persons with an incomplete TB treatment history. DOT is also highly recommended for patients who require translation services.
  - For patients 16 years of age and older at **low risk** of progression to TB, a combination of DOT and SAT may be considered, with each DOT visit including an in-person assessment of treatment compliance and side effects. Doses one, two, six and 10 of 3HP are provided via DOT with the patient self-

administering doses three through five, seven through nine, and doses 11 and 12. Patients should have a final clinic visit upon completion of treatment.
    - A combination of in-person DOT and video DOT may be used for patients meeting video DOT eligibility criteria.
    - All patients on the DOT+SAT regimen will maintain a medication diary and record any side effects.
- The 3HP regimen is not approved for use by pregnant women.

Physicians treating patients for LTBI are encouraged to review the updated recommendations of both the CDC and the TB Program and should determine how to best implement the new guidelines in their practice or clinic.

Other Information

The updated CDC recommendations also include the following information:

- Approximately 5% of patients discontinue 3HP because of adverse events. Side effects typically occur after the first three to four doses and usually resolve without treatment within 24 hours. However, if symptoms suggestive of a systemic drug reaction occur[iv], patients should stop using 3HP while the underlying cause is determined.
- Data published since 2011 confirm the effectiveness of 3HP in individuals with HIV infection who are not taking antiretroviral therapy and demonstrate the absence of clinically significant drug interactions between once-weekly rifapentine and either efavirenz or raltegravir in individuals with HIV infection treated with those antiretroviral medications. Simultaneous use of LTBI treatment and antiretroviral medications in patients with HIV infection should be guided by clinicians experienced in managing both conditions.

Clinicians with questions about 3HP or regarding a specific patient can call the TB Program at 717-787-6267 to request a consultation.

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[i] Centers for Disease Control and Prevention (CDC). Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent *Mycobacterium tuberculosis* infection. *MMWR Morb Mortal Wkly Rep.* 2018;67(25):723-726.

[ii] Njie GJ, Morris SB, Woodruff RY, Moro RN, Vernon AA, Borisov AS. Isoniazid-rifapentine for latent tuberculosis infection: a systematic review and meta-analysis. Am J Prev Med 2018. Epub June 11, 2018. https://doi.org/10.1016/j.amepre.2018.04.030

[iii] Groups at higher risk of progression to TB disease include, but are not limited to, children less than 5 years of age; persons with HIV infection; persons infected with Mycobacterium tuberculosis within the last 2 years; foreign-born persons; and persons with other immunocompromising conditions such as diabetes, end stage renal disease, or organ transplantation.

[iv] Such as fever, headache, dizziness, nausea, muscle and bone pain, rash and itching