NTCA PROVIDER GUIDANCE:

Using the Isoniazid/Rifapentine Regimen to Treat Latent Tuberculosis Infection (LTBI)

IMPORTANT NOTE: *Rule out* **active** *TB disease in all persons prior to initiating treatment for LTBI.*

What is the 12-dose isoniazid/rifapentine regimen (aka "3HP")?

The 3HP regimen consists of 12 once-weekly doses of isoniazid (H) and rifapentine (Priftin®) (P). It provides a safe and effective treatment for LTBI. Rifapentine is a member of the rifamycin class and has many of the same drug-to-drug interactions and side effects as other rifamycins.

What are the advantages of 3HP?

- The 12-dose regimen reduces treatment time by two-thirds (9 months to 3 months) compared to isoniazid.
- Shorter treatment regimens have been shown to have higher rates of completion.
- Weekly dosing offers convenience for many individuals.
- There are lower rates of hepatotoxicity with 3HP than with daily doses of isoniazid.

What are the doses?

Drug*	Weekly Dosage	Maximum dose
Isoniazid 	15 mg/kg rounded to nearest 50/100mg in patients ≥ 12 years	900 mg
	25 mg/kg rounded to the nearest 50/100 mg in patients 2–11 years	
Rifapentine (Priftin®) 	10.0 – 14.0 kg = 300 mg	900 mg
	14.1 – 25.0 kg = 450 mg	
	25.1 – 32.0 kg = 600 mg	
	32.1 – 49.9 kg = 750 mg	

**Tablets can be crushed and administered with semi-solid food for those unable to swallow pills.*

Who is not recommended for treatment with 3HP?

- Children under 2 years of age
- Patients with potential for severe or unmanageable drug interactions, including people living with HIV or AIDS on certain antiretroviral therapy regimens
- Persons presumed infected with *M. tuberculosis* that is resistant to isoniazid and/or rifampin
- Pregnant women or women planning to become pregnant during treatment
- Patients who had prior adverse events or hypersensitivity to isoniazid or rifampin or rifapentine

ALERTS:

- Do not confuse **rifampin/rifabutin** with **rifapentine** (Priftin®).
- Patients who weigh ≥ 50kg should take 6 tablets of rifapentine and 3 tablets of isoniazid for a total of 9 pills at a time.
- Some TB experts recommend prescribing vitamin B6 with this regimen due to concerns regarding isoniazid-induced peripheral neuropathy.
- If 3HP is self-administered, it is imperative that the patient understands the directions to take all of the pills in the weekly dose at the same time. **The patient should not split doses.**
- If symptoms suggestive of a systemic drug reaction occur, the patient should stop 3HP while the cause is determined.
- Doses should be given at least 72 hours apart and, per expert opinion, there should be no more than 3 doses in 18 days.
- Different from other rifamycins, rifapentine can be taken with food to increase absorption.
- Maintain adequate hydration.

What is completion of therapy?

- Completion of therapy is 12 doses taken in 16 weeks.

NOTE: *Near the end of the treatment period, the TB clinician may consider completion of therapy for TBI with only 11 once-weekly doses within a 16-week period under rare and insurmountable circumstances in which the patient cannot take an additional (12th) dose.*

Does this regimen have to be administered via directly observed therapy (DOT)?

- DOT ensures the highest quality and safety of treatment, and confirms that treatment is completed.
- The healthcare provider should choose the mode of administration, i.e., either DOT versus self-administered therapy (SAT) based on local practice and individual patient attributes and preferences. It is critically important for the clinician to assess the patient's ability to understand risks associated with treatment and procedures to follow if a side effect is suspected, as well as the risk for progression to severe forms of TB disease.

How frequently were toxicities observed with 3HP?

Hypersensitivity *including flu-like symptoms, headaches, hypotension, near-syncope/syncope*	3.8%
Rash	0.8%
Hepatotoxicity	0.4%
Thrombocytopenia	infrequent
Other toxicities	3.2%

NOTE: *Refer to the product insert for a full list of potential side effects. Most side effects occur in the first 4 weeks, although they can continue to occur throughout treatment.*

What can an adverse event include and how should I respond?

	Adverse Event		Response
Moderate to Severe	• Hypersensitivity • Hypotension • Dizziness or nausea/vomiting *(these can be prodrome to syncope)* • Syncope/fainting • Hospitalization • Life-threatening event • Flu-like syndrome *(e.g., fever, chills, headaches, dizziness, musculoskeletal pain)* • Thrombocytopenia	• Shortness of breath • Wheezing • Acute bronchospasm • Urticaria • Petechiae • Purpura • Conjunctivitis • Angioedema • Shock	**Discontinue treatment** **Conduct prompt clinical assessment with appropriate lab monitoring**
Mild to Moderate	• Rash • Fever • Pruritus		**Continue to monitor the patient closely with a low threshold for discontinuing treatment**

How do I report an adverse event regarding 3HP?

- Report all adverse events to FDA MedWatch at **www.fda.gov/Safety/MedWatch/default.htm. 1-888-INFO-FDA (1-888-463-6332)**
- Report adverse events leading to death or hospitalization to your health department. Health departments should report these adverse events to the Centers for Disease Control and Prevention at **1-800-232-4636** or **LTBIdrugevents@cdc.gov**

Are there drug-drug interactions?

Yes, there are common interactions for isoniazid and rifapentine:

- **Isoniazid** increases blood levels of phenytoin and disulfiram.
- **Rifapentine** decreases blood levels of oral or implanted hormonal contraceptives, warfarin, sulfonylureas, methadone, steroids, some cardiac medications, and certain antiretroviral therapy regimens may have serious drug interactions.

NOTE: *Use a drug interactions checker and/or refer to the product insert for a full list of drug-drug interactions.*

Whom do I contact with questions or concerns?

- Contact your local or state health department.
- NTCA has an online directory of TB programs at **http://www.tbcontrollers.org/community/statecityterritory/**

What type of monitoring do I need to do?

- Evaluate the patient at a monthly visit to identify adverse events and to assess treatment adherence.
- Some experts recommend baseline complete blood count (CBC) due to a possible adverse reaction decreasing the white blood cell count and platelet counts and comprehensive metabolic panel (CMP). Hepatitis panel may also be obtained.
- Baseline hepatic chemistry is recommended for patients with these specific conditions:
  - HIV infection
  - Liver disorders
  - In the postpartum period (≤ 3 months after delivery)
  - Regular alcohol or injection drug use

  In addition, consider baseline hepatic chemistry for older persons and for persons taking medications for chronic medical conditions.
- If baseline hepatic chemistry testing is abnormal, determine the risk vs. benefit of treatment. If a decision is made to treat, continue with subsequent hepatic chemistry testing until the patient is determined to be stable.
- If baseline hepatic chemistry is within normal limits and the treatment is self-administered, some experts recommend additional laboratory monitoring monthly to ensure that the patient does not develop hepatotoxicity.
- When or after the final dose is taken, conduct a final visit with the patient to monitor for any adverse events.

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For references, go to http://www.tbcontrollers.org/resources/3hp