

## Virginia Guidelines for the Use of Isoniazid/Rifapentine (3HP) for the Treatment of Latent TB Infection in Health Department Settings

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## Preventing Tuberculosis

- ▶ Treatment for latent TB infection is the cornerstone of the US strategy for TB elimination
- ▶ Active TB develops in 5–10% of individuals who are infected with TB
- ▶ Those with impaired cellular immunity are at higher risk for developing active TB

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## Latent TB Infection Therapy

- ▶ Isoniazid:
  - 9 months of treatment
- ▶ Pros:
  - Inexpensive
  - Best efficacy and safety data
    - Hepatitis in 0.1–0.6% of patients
    - About 75–80% effective
- ▶ Cons:
  - low completion rates of 30–64%

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### Other LTBI Treatment Options

- ▶ Rifampin:
  - 4 months of therapy
  - when used
    - contact to INH-resistant disease
    - INH contraindicated
    - not tolerated by the patient
    - Not used just to get it done in shorter time period
- ▶ Rifampin/PZA:
  - not recommended due to hepatotoxicity

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### PREVENT TB Trial

- ▶ Enrolled 8,053 patients
- ▶ Most participants were from the US and Canada, some from Spain and Brazil
- ▶ Participants either received 9 months of INH or a once-weekly dose of rifapentine and isoniazid for 3 months given via DOT
- ▶ Trial lasted for 10 years and participants were followed for approximately 33 months to evaluate for development of TB disease

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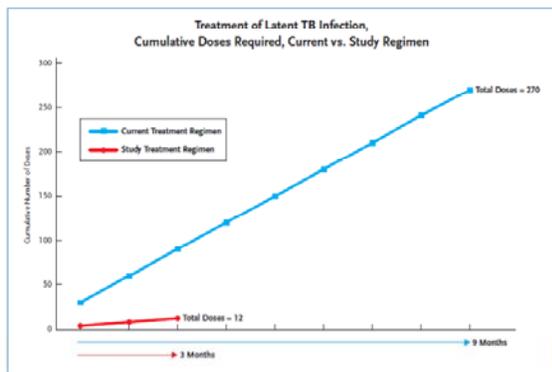
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### PREVENT TB Trial

- ▶ Completion of INH-RPT was defined as 11 or 12 doses within 16 weeks
- ▶ Doses had to be separated by >72 hours to be counted

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### 12-Weeks of once weekly INH/Rifapentine (1)

- Pros:
- ▶ Shorter duration of treatment (12 doses vs. 270 doses)
  - ▶ Individuals more likely to complete therapy (82% vs 69%)
  - ▶ 7 cases of TB in INH-Rifapentine group vs. 15 cases in INH group
  - ▶ Similar amount of adverse drug events in each group

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### 12-Weeks of once weekly INH/Rifapentine (2)

- Cons:
- ▶ More Expensive: \$503 vs \$237
  - ▶ May have difficulty getting Rifapentine
  - ▶ Trial results are applicable only in low-to-medium TB incidence countries
  - ▶ Not clear how to use this regimen in special populations:
    - HIV positive
    - Children under 5

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Morbidity and Mortality Weekly Report

Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection

- ▶ INH-RPT given as 12 weekly DOT doses is recommended as an equal alternative to 9 months of daily self-supervised INH for treating LTBI in otherwise healthy patients
  - aged  $\geq$  12 years at risk for TB disease
  - recent exposure to contagious TB
  - conversion of TST or IGRA
  - radiographic findings of healed pulmonary TB

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**Choosing between INH and INH-RPT**

- ▶ Feasibility of DOT
- ▶ Resources available for obtaining drugs
- ▶ Ability of the program to monitor patient
- ▶ Expectance of treatment completion based on medical/social circumstances
- ▶ Preferences of the patient and the prescribing physician

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**INH-RPT NOT Recommended**

- ▶ Children <2 years old
- ▶ HIV-infected patients receiving HAART
- ▶ Pregnant women and women expecting to become pregnant during treatment
- ▶ Where LTBI is presumed to have INH or RIF resistance

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## Children

- ▶ Preferred regimen for children aged 2–11 years: 9 months of INH
- ▶ However, INH–RPT may be considered on a case–by–case basis when BOTH:
  - 1) completion of 9 months of therapy is unlikely
  - 2) the likelihood or hazard of TB is great

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## Dosing

**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/study00023452?term=rifapentine&rank=9>.

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## Rifapentine (1)

- ▶ Longer half life than rifampin
- ▶ Orange discoloration of secretions, urine, tears
- ▶ Can stain contact lenses
- ▶ Rare adverse effects:
  - elevated liver function tests
  - thrombocytopenia
  - headache and dizziness

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### Rifapentine (2)

- ▶ Increases the metabolism of medications, particularly those metabolized by cytochrome P450 3A:
  - birth control
  - coumadin
  - methadone
  - glipizide, glimepiride, glyburide (oral diabetes)
  - levothyroxine (thyroid medicine)

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### Directly-observed therapy

- ▶ DOT recommended
- ▶ Missed doses or altered dosing intervals
  - can affect effectiveness
  - Safety, i.e. side effects or toxic reactions

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### Monitoring (1)

- ▶ At each encounter, patients need to be asked if they have:
  - fever
  - yellow eyes (jaundice)
  - dizziness
  - rash
  - aches
  - >1 day of nausea, vomiting, weakness, abdominal pain or loss of appetite
- ▶ If yes - contact case manager immediately!
  - Do not give dose until cleared

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### Monitoring (2)

- ▶ Monthly clinical assessments, to include inquiries about side effects and a physical examination by clinician or nurse case manager
- ▶ Laboratory tests:
  - baseline LFTS for
    - HIV
    - liver disease
    - ETOH use
    - immediate post-partum period
  - repeat liver tests
    - those with baseline abnormal tests
    - those at risk for liver disease

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### Virginia Specific Guidelines

- ▶ Posted on the VDH TB Control website
  - Resources for Local Health Departments/Policies
- ▶ Included:
  - Who the regimen is recommended for as well as contraindications
  - Dosing
  - Monitoring recommendations

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### Virginia Specific Guidelines

- ▶ DOT mandatory for this regimen
- ▶ Completion defined as 11 or 12 doses within 16 weeks
- ▶ "Weekly" doses must be separated by > 72 hours to be countable

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### Individual Drug Pricing

- ▶ Isoniazid 300 mg– \$.09/tab
- ▶ Isoniazid 100 mg – \$.06/tab
- ▶ Pyridoxine 50 mg – \$.08/tab
- ▶ Rifapentine/Priftin 150mg – \$2.48/tab
  - New formulations with larger dose and fixed dose combinations in development
  - Price has dropped and will continue to drop




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### Approximate Current Pricing

Client Weight	INH Dose	Priftin Dose	# of Priftin	Weekly Cost	Regimen Cost
10.0–14.0 kg	150–250 mg	300 mg	2	\$5.14	\$61.80
14.1–25.0 kg	250–400 mg	450 mg	3	\$7.68	\$92.16
25.1–32.0 kg	400–500 mg	600 mg	4	\$10.22	\$122.64
32.1–49.9 kg	500–750 mg	750 mg	5	\$12.70	\$152.52
≥ 50.0 kg (≥ 110 lb)	750 mg+ (900 mg max)	900 mg (max)	6	\$15.15	\$181.80

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### Post implementation Follow-up

- ▶ Notify TB Control if clients placed on 3HP
- ▶ Call TB Control for any client on 3HP with adverse reactions that are hospitalized or die.
  - Special reports that must be completed
  - 804-864-7906

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