



Indian Health Service
IHS National Pharmacy and Therapeutics Committee
Formulary Brief: 12 Week Rifapentine Regimen in
Treatment of Latent Tuberculosis Infection
September 2013



Background:

The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed recent clinical data concerning the use of the drug rifapentine, an antimycobacterial rifamycin derivative, in the treatment of pulmonary tuberculosis at their August 2013 meeting. Based on the information presented, the committee **added** rifapentine to the IHS National Core Formulary (NCF).

Discussion:

Pulmonary tuberculosis is transmitted via airborne droplets from patients infected with active *Mycobacterium tuberculosis* disease. Once infected, the mycobacterium may remain in the host in a latent state for decades before disease activation, though half of these patients will develop active disease in the first two years. The use of antituberculosis regimens during this period can prevent active disease from developing in these patients.¹ Recent clinical data has suggested a 3 month regimen containing rifapentine utilizing directly observed therapy (DOT) may be useful in latent tuberculosis infections providing a regimen with decreased treatment duration, increased tolerability, and increased adherence.

In 2011, Sterling et al. published results on an open-label, randomized, non-inferiority trial comparing the efficacy and safety of a 12 week, once weekly treatment of isoniazid (INH) and rifapentine under DOT with that of 9 months of daily, self-administered INH. The combination group received 900 mg rifapentine and 15-25 mg/kg (rounded up to nearest 50 mg, 900 mg max) INH. Daily INH was administered at 5-15 mg/kg (rounded up to nearest 50 mg, 300 mg max). They found combination therapy to be non-inferior to the daily INH standard of treatment. Patients on combination therapy had higher rates of treatment completion than those on daily INH (82.1% vs 69%, $P < 0.001$).²

In 2011, Martinson et al. reported findings of their open-label, randomized trial comparing efficacy and safety of 4 treatment regimens (3 study groups, 1 control group) in preventing tuberculosis in 1,148 HIV-infected individuals. The treatment groups were regimens of once weekly 900 mg rifapentine plus 900 mg INH for 12 weeks under DOT, twice weekly 600 mg rifampin plus 900 mg INH for 12 weeks, 300 mg INH daily for 6 years, and a control regimen of 300 mg daily INH for 6 months. Adherence rates were highest for patients receiving rifapentine and INH with 95.7% of patients completing at least 90% of doses. The incidences of tuberculosis in patients across all treatment groups were not statistically different from that of the control group concluding the regimens had similar efficacy. The researchers reported no statistically significant safety issues with the rifapentine and INH regimen.³

In 2006, Schechter et al. reported results of their randomized, controlled clinical trial comparing 900 mg rifapentine and 900 mg INH once weekly for 12 weeks under DOT to a control regimen of either 450 mg rifampin and 750 mg pyrazinamide for patients weighing < 50 kg or 600 mg rifampin and 1,500 mg pyrazinamide for patients weighing ≥ 50 kg. Rifampin/pyrazinamide treatment durations were 8 weeks. The trial was discontinued prematurely due to increased incidences of hepatotoxicity with the rifampin/pyrazinamide treatment group. However, only 1.46% of patients receiving rifapentine and INH developed active TB which was below the accepted target of $< 4\%$. The rifapentine/INH regimen had a favorable tolerability profile during the duration of the experiment.⁴

Findings:

The IHS NPTC finds good evidence exists to support and encourage the use of rifapentine in combination with INH once weekly for 12 weeks under DOT as a viable and efficacious option for the treatment of latent tuberculosis infection. Due to the shorter duration of therapy utilizing DOT, adherence rates for this regimen

are higher than those seen with other accepted regimens. This coincides with a higher percentage of these patients completing therapy. The safety profile of this treatment regimen shows the regimen is well tolerated.

References

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2. Sterling TR, Villarino ME, Borisov AS et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. *The New England Journal of Medicine*. 2011; 365(23): 2155-2166.
3. Martinson NA, Barnes GL, Moulton LH et al. New regimens to prevent tuberculosis in adults with HIV infection. *The New England Journal of Medicine*. 2011; 365(1): 11-20.
4. Schechter M, Zajdenverg R, Falco G et al. Weekly rifapentine/isoniazid or daily rifampin/pyrazinamide for latent tuberculosis in household contacts. *American Journal of Respiratory and Critical Care Medicine*. 2006; 173: 922-926.