INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: *Tuberculosis Treatment (Update)*
-April 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a clinical update on drug regimens used to treat pulmonary tuberculosis. Medications currently listed on the IHS National Core Formulary (NCF) for the treatment of latent and active pulmonary tuberculosis include ethambutol, isoniazid, pyrazinamide, rifampin, and rifapentine. In January 2025, U.S.-based guidelines were updated and recommended isoniazid, rifapentine, pyrazinamide, and moxifloxacin for a treatment duration of 4 months for drug-susceptible pulmonary tuberculosis.[1] This review examines current literature and recent guideline updates for drug-susceptible and drug-resistant pulmonary tuberculosis. Following clinical review and analysis, the NPTC voted to **ADD moxifloxacin "for use in tuberculosis (TB) treatment only, in consultation with a TB specialist" to the NCF.**

Discussion:

Mycobacterium tuberculosis is a rod shaped, slow growing, acid-fast bacteria that causes tuberculosis. The American Indian/Alaska Native (AI/AN) population currently has the second highest incidence rate among U.S. born persons.[3] This stresses the importance of ensuring access to currently recommended medications for the treatment of TB across the IHS system of care. There are two types of pulmonary TB, latent (also known as tuberculosis infection, or TBI) and active disease. There has been no change in treatment recommendations for latent TB since 2020.[4]

Drug-Susceptible Pulmonary TB (DS-TB): Prior to the new update, the 2016 guideline recommendations from the American Thoracic Society, U.S. Centers for Disease Control and Prevention, European Respiratory Society, and Infectious Diseases Society of America (ATS/CDC/IDSA) for DS-TB was a 6-month regimen of rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE).[2] In 2021, Dorman et al. published an international, multicenter, randomized, controlled trial (RCT) that evaluated the use of rifapentine-containing regimens, with or without moxifloxacin (RPT-MOX, RPT) for 4 months compared to standard RIPE therapy for 6 months.[5] The study included 2,343 patients who were 12 years and older with newly diagnosed pulmonary TB that were susceptible to rifampin, isoniazid, and fluoroquinolones. The goal was to determine if 4 months of the rifapentine regimens were non-inferior to standard RIPE therapy. Efficacy was determined by survival-free TB 12 months after randomization and safety was evaluated by the number of adverse events that were grade 3 or higher. Study results yielded that RPT for 4 months was inferior to RIPE therapy for 6 months (14.2% vs. 9.6%, 95% CI: 1.2 to 7.7). However, RPT-MOX was found to be non-inferior (11.6% vs 9.6%, 95% CI: -1.1 to 5.1). An unfavorable outcome, such as TB recurrence, occurred in 6% of population receiving RPT-MOX vs. 3.3% of the population receiving RIPE therapy. In terms of safety, there was no difference between RPT-MOX and RIPE therapy (18.8% vs. 19.3%, 95% CI: -4.3 to 3.2). The authors concluded that 4 months of treatment with rifapentine, isoniazid, pyrazinamide, and moxifloxacin was non-inferior to 6 months of traditional RIPE therapy and that adverse events were similar between the regimens. Short-course TB treatment regimens were reviewed at the Spring 2024 NPTC meeting, however at that time, there had been no updates in clinical practice guidelines and no changes were made to the NCF. In January 2025, the ATS/CDC/ERS/IDSA guidelines were published with the following recommendation: 4 months of treatment with isoniazid, rifapentine, moxifloxacin, and pyrazinamide is conditionally recommended for adults and adolescents (12 years and older) with drug-susceptible pulmonary tuberculosis.[1] This conditional recommendation referenced the 2021 Dorman et al. study as supporting evidence. In order to support TB specialists within IHS in the treatment of drug-susceptible pulmonary TB, moxifloxacin was added to the NCF.

Drug-Resistant Pulmonary TB (DR-TB): New medication regimens are continuing to emerge for DR-TB. Similar to DS-TB, updated guidelines recommended shorter treatment durations with newer regimens. Prior to the recent guideline update, the 2019 ATS/CDC/ERS/IDSA recommended a treatment duration of 15 months, however in 2022, the World Health Organization (WHO) changed their recommendation to 9 months.[6-7] In 2022, Nyang'wa et al. published a phase 2-3, multicenter, RCT entitled as "TB- PRACTECAL".[8] Stage 1 was

to determine which regimen should move to stage 2, to be compared against the standard-care (regimens recommended by the WHO). BPaL (bedaquiline, pretomanid, and linezolid), BPaLC (BPaL + clofazimine) and BPaLM (BPaL + moxifloxacin) were evaluated to determine the percentage of patients that would experience culture conversion 8 weeks post randomization. BPaLM was chosen to move to stage 2, which evaluated the efficacy and safety of a 6-month regimen compared to a 9-to-20-month standard-care regimen. Patients were included if they were >15 years of age with rifampin resistant pulmonary TB. Primary efficacy was an unfavorable outcome at 72 weeks post randomization and safety was ≥1serious adverse event at 3 different time points throughout the trial. BPaLM was non-inferior and superior to standard care in the modified intention-to-treat population with 11% vs. 48% experiencing an unfavorable outcome [Risk Difference: -37, 95% CI: -53 to -22]. For safety outcomes, BPaLM was also found to be non-inferior to the standard-care arm for all 3 time points.

Conradie et al. published a partially blinded, randomized trial evaluating the use of BPaL (linezolid 1,200mg for 26 weeks vs. 1,200mg for 9 weeks vs. 600mg for 26 weeks vs. 600mg for 9 weeks) for those ≥14 years of age with extensively drug-resistant TB (XDR-TB), pre XDR-TB, and rifampin-resistant TB. There was no control arm in this study and 181 patients were included. Favorable outcomes occurred in all 4 treatment groups and were considered significant. Authors reported the following results for each treatment arm: linezolid 1,200mg x 26 weeks = 93% (95% CI: 81-99%); linezolid 1,200mg x 9 weeks = 89% (95% CI: 76-96%); linezolid 600mg x 26 weeks = 91% (95% CI: 79-98%) and linezolid 600mg x 9 weeks = 84% (95% CI: 70-93%). Higher incidence of adverse effects and dose modifications were observed in groups that received 1,200mg of linezolid while the treatment group who received linezolid 600mg for 9 weeks experienced the highest incidence of unfavorable outcomes (16%). When comparing all regimens for safety and efficacy for DR-TB, linezolid 600mg for 26 weeks was determined to be more favorable.[9]

Both of the trials referenced above were included in the ATS/CDC/ERS/IDSA clinical practice guidelines for the treatment of DR-TB, which were released in January 2025:

1. Adults and adolescents (≥14 years of age) with rifampin-resistant, fluoroquinolone-resistant (or intolerance) pulmonary TB with either no exposure to bedaquiline and linezolid or exposure less than 1 month:

Treatment: Bedaquiline, pretomanid, and linezolid (BPaL) for a treatment duration of 6 months (strong recommendation).

2. Adults and adolescents (14 years and older) with rifampin resistant, fluoroquinolone susceptible pulmonary TB:

Treatment: Bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM), duration of 6 months (strong recommendation).

Findings:

The addition of moxifloxacin to the IHS NCF is supported by current ATS/CDC/ERS/IDSA guidelines for the treatment of drug-susceptible pulmonary TB. The NPTC included that moxifloxacin was added solely "for use in tuberculosis (TB) treatment only, in consultation with a TB Specialist," in an effort to reserve its use and prevent fluoroquinolone resistance. When treating drug-resistant pulmonary TB, a TB medical expert consultation is recommended. Currently, there is no evidence of drug-resistant TB within the IHS. Therefore, no changes were recommended for the NCF for the treatment of drug-resistant TB.

References:

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