Abstract: *Linezolid dosing and pharmacokinetics in North American patients with tuberculosis, 2019-2023*

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Introduction*:* Linezolid is recommended in treatment regimens for multi-drug-resistant tuberculosis. However, considerable pharmacokinetic variability exists and long-term use is limited by adverse effects. This study evaluates the pharmacokinetics of linezolid in patients with tuberculosis from an international therapeutic drug monitoring service.

Methods: Linezolid trough, 2-hour, and 6-hour post-dose samples from across North America were tested by the University of Florida Infectious Disease Pharmacokinetics Laboratory. Total serum concentrations were measured using liquid chromatography-tandem mass spectrometry. Therapeutic drug monitoring was performed, and measurements were compared to typical linezolid concentrations including a trough value of <2 mcg/mL and peak value between 12-26 mcg/mL.

Results: From January 2019 to December 2023, 1604 linezolid samples from 500 patients and 817 unique TDM occasions were analyzed. Trough concentrations were measured on 670 samples (median 1.19 mcg/mL [range 0.00-20.06]), and 232 troughs (34.6%) were >2 mcg/mL. Among trough samples from linezolid dosing of 600mg daily or 5 days/weekly, 43.2% were >2 mcg/ml. Of 600 available peak samples, 264 (44%) were outside typical range, most (89%) being <12 mcg/mL.

Conclusion*:* High serum linezolid trough concentrations were measured in approximately one-third of samples and in more than 40% of those taking the recommended dose. More than 40% of peak concentrations were measured outside the typical range. This study demonstrates that therapeutic drug monitoring can be used to identify patients with serum linezolid concentrations outside of targeted ranges, allowing clinicians to make appropriate dose adjustments to improve outcomes.