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Title: **Telavancin use in Hospitalized Patients with Diminished Renal Clearance**

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PURPOSE: Telavancin is a lipoglycopeptide antibiotic with potent activity against Gram-positive organisms, including methicillin-resistant Staphylococcus aureus (MRSA). It is often reserved for patients with infections refractory to vancomycin or in cases where reduced susceptibility limits treatment options. Additionally, its activity against biofilms makes it an attractive agent for prosthetic hardware infections. However, telavancin has been associated with acute kidney injury (AKI), leading to FDA warnings and cautious use in patients with impaired renal function. The antibiotic's prescribing information notes a higher incidence of nephrotoxicity in phase III trials, particularly in patients with preexisting renal dysfunction (CrCl <50 mL/min). This has contributed to reserving telavancin in clinical practice when alternative therapies are available. Despite these concerns, some evidence suggests that telavancin remains a viable option when alternative therapies fail. Studies, including post-marketing surveillance data, indicate that the observed nephrotoxicity may not be as clinically significant in all cases, particularly in carefully selected patients. Moreover, telavancin's rapid bactericidal activity and potential efficacy in difficult-to-treat infections warrant a re-evaluation of its utility in patients with renal dysfunction. The purpose of this study is to assess telavancin use in hospitalized patients with pre-existing renal dysfunction who failed prior antibiotics, with a focus on any changes in renal clearance as well as patient outcomes.

METHODS: The retrospective cohort study evaluated patients who received at least 3 doses of telavancin over 3 days and had a pre-existing creatinine clearance (CrCl) of less than 60 mL/min with a serum creatinine of 1.3 mg/dL or greater. Patients were identified from a generated report using Cerner Discern Analytics 2.0 between January 2018 and May 2024. Those on dialysis prior to receiving telavancin were excluded. Medical records were reviewed for pertinent data including patient demographics, telavancin dosage, duration of therapy, infection type, prior antibiotic use, and concomitant nephrotoxins. Renal function and CrCl were evaluated for each patient throughout their course of treatment. Patient outcomes and response to antibiotic therapy

were determined based on investigator assessment, utilizing appropriate monitoring parameters, considering the infection type, along with provider progress notes. Approval by the hospital institutional review board was obtained for this project.

Results/Conclusion: A total of 34 patients were included in this evaluation of patients with pre-existing renal dysfunction. Renal function did not worsen in 82% of patients at the end of telavancin treatment (EOTT), with improved renal function documented in most patients. Approximately 18% of patients had an increased SCr at the EOTT. The improved CrCl in patients on telavancin therapy was likely related to their overall clinical improvement. Over 85% of our inpatients failed at least one prior antibiotic, and 76.5% were not responding to antibiotic treatment for Gram (+) bacteremia before starting telavancin. Standard telavancin dosing is 10mg/kg daily. At ARMC, a lower dosage of telavancin has been utilized (7.5-8 mg/kg) based on clinical evidence, which may have impacted our findings, as AKI is dose related. Patients received an average of 8 mg/kg of telavancin and approximately 74% had a positive clinical outcome. In our study, telavancin appears to be an effective antibiotic treatment for those with diminished renal dysfunction. A 74% positive clinical response rate demonstrates the value telavancin may provide in hospitalized patients. Study findings demonstrate that telavancin is an effective option for inpatients with serious Gram positive infections despite concerns for renal toxicity. Response to telavancin may result in an improvement of renal function.

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