

# Single dose Linezolid Pharmacokinetics in ill Patients with Impaired Renal Function Especially Chronic Hemodialysis Patients

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## **Abstract**

**ABSTRACT:** Background and Objective: Renal failure patients were treated with linezolid (LZD) for proven or suspected infections by multi-resistant Gram-positive cocci. The aim of this study was to determine if dose adjustment of LZD is needed as a function of renal impairment or not, especially that a significant component of LZD is eliminated unchanged in urine. Methods: The single dose pharmacokinetics of LZD was investigated. Eighteen non-infected male subjects with various degrees of renal impairment ranged from normal to severe chronic impairment were enrolled, including end-stage renal disease (ESRD) patients maintained on hemodialysis (HD). LZD was administered as a single oral 600mg dose, and blood samples were drawn at different times and analysed by a validated HPLC assay method. Plasma profiles were evaluated by non-compartmental and compartmental approaches. Results and Discussion: A similar rate and extent of LZD absorption and elimination and comparable body exposure was observed in both healthy subjects and acute renal failure patients. The extent of LZD exposure was significantly increased by 3-fold in ESRD patients in their off-dialysis day. Furthermore, the  $t_{1/2}$  and MRT values were significantly increased by ~5- and 3-fold, respectively. The  $V_d/F$  values of LZD did not change with renal function. A significant decrease in  $CL/F$  by ~3-fold was observed in ESRD patients in their off-dialysis day however,  $CL/F$  was significantly increased by ~4-fold during HD. Approximately half of the administered LZD dose was removed during the HD session in these selected cohorts of ESRD

patients. LZD was generally well tolerated. Conclusions: The dose of LZD did not need to be adjusted for patients with acute renal dysfunction or ESRD on HD. One of the twice-daily doses should be administered after the dialysis session because almost half of the LZD dose was substantially removed by HD. During the first three dialysis sessions of the treatment course, to avoid potentially ineffective therapy, a supplemental dose of LZD might be given if necessary or the dose of LZD should be administered 4 h before the beginning of the HD session. This was to keep LZD levels above the MIC for the organism causing the infection being treated.

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