**Cost-Efficiency and optimization of cefiderocol dosing: Insights from population pharmacokinetic/pharmacodynamic simulation.**

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**Background:** Cefiderocol stands as a potent siderophore cephalosporin with marked activity against carbapenem-resistant Enterobacterales. Given its significant cost—$232.25 per vial in the United States and ¥20,203 in Japan—the development of an efficient dosing strategy is crucial. This study evaluated the potential for medical cost reduction through identification of lower, yet effective, dosing regimens utilizing the Monte Carlo simulation technique.

**Methods:** Employing a virtual population of 10,000, resampled according to a pre-established population pharmacokinetic (popPK) model, this simulation aimed to identify the optimal time for unbound cefiderocol concentration to remain above the minimum inhibitory concentration (TAM_unbound) at 100%, leveraging an MIC distribution or specified value for maximal bactericidal effect.

**Results:** Nearly 100% probabilities of reaching the desired TAM_unbound with standard, lower (reduced by 1 g or 1 dose), and extended low (reduced by 2 g or 2 doses) dosing regimens were observed. Notably, the extended low dosing regimen exhibited the lowest probability of achieving the TAM_unbound target (86.4%) in patients with a creatinine clearance (CCr) range of 90-120 mL/min. For MICs of ≤0.5 μg/mL, the probability of achieving TAM_unbound at 100% exceeded 90% with the extended low dosing regimen. By adopting an efficient dosing approach, the cost over a 10-day treatment period for 10 patients was approximately reduced half, from $122,826.50 to $62,665.69 in the United States and ¥12,598,187 to ¥5,451,173 in Japan.

**Conclusions:** The findings advocate for consideration of lower dosing regimens of cefiderocol as a strategy for substantial medical cost reduction. Therapeutic drug monitoring might be integral to the successful application of such regimens, underscoring the need for further clinical validation.

**Keywords:** Cefiderocol; Population Pharmacokinetics; Pharmacodynamics; Simulation; Cost Efficiency; Therapeutic Drug Monitoring