

- Cefazolin penetration into the interstitial fluid of a lower limb infection varied across this simulated patient population.
- Cefazolin 1 g every eight hours (q8h) % $fT > MIC$ (the percent of the dosing interval that free drug concentrations remained above the minimum inhibitory concentration) exposures in serum were high at MICs of 1 mg/L and 2 mg/L.
- Based on the tissue exposure, 1 g q8h dose regimen should be sufficient to achieve 30% $fT > MIC$ target against most methicillin-susceptible *Staphylococcus aureus* causing complicated skin and soft tissue infections (cSSTI).
- For Enterobacteriaceae with MIC of 2 mg/L, the probability of target attainment (PTA) for the established 50% $fT > MIC$ target, were not optimal with 1 g q8h dose.
- At least 2 g q8h is required to achieve PTA of $\geq 80\%$ when treating cSSTI caused by susceptible Enterobacteriaceae (MIC ≤ 2 mg/L).

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