

Change in preferred anti-pseudomonal agent from piperacillin-tazobactam to cefepime or ceftazidime when used concomitantly with vancomycin

Situation	Emerging data shows that concomitant vancomycin with piperacillin-tazobactam (P/T) independently increases the risk of acute kidney injury (AKI) in patients compared to vancomycin alone or vancomycin with another β -lactam (e.g. cefepime or a carbapenem).
Background	A systematic review and meta-analyses of 3,549 patients found a more than 3-fold increased risk of AKI in the vancomycin and P/T arm, ¹ while another involving over 24,000 patients found a 22.2% rate of AKI vs.12.9% (NNH =11) for comparators (vancomycin alone \pm β -lactams or carbapenem). ² The median onset of AKI was reported at 3 to 5 days in those who received vancomycin with P/T. ^{3,4}
Assessment	To limit the risk of AKI, this combination should be avoided if suitable alternatives exist. Epic changes are planned this fall.
Recommendation	<ul style="list-style-type: none"> • If anti-pseudomonal coverage is indicated, use cefepime or ceftazidime in place of piperacillin-tazobactam for patients receiving vancomycin <ul style="list-style-type: none"> ○ If anaerobic coverage is indicated, supplement with metronidazole • Reassess if empiric anti-pseudomonal, anti-MRSA coverage is warranted. <ul style="list-style-type: none"> ○ Use of P/T is frequently inappropriate in most cases of community-acquired pneumonia and cellulitis • De-escalate early. Perform a formal antibiotic time-out at 48-72 hours in conjunction with daily reassessments of the initial empiric regimen <p>Resources:</p> <ol style="list-style-type: none"> 1. SHC sepsis guide (internal link) (external link) 2. SHC antibiogram - link 3. Antibiotic Stewardship website (internal link) (external link)

References:

1. Hammond DA, et al. Systematic review and meta-analysis of acute kidney injury associated with concomitant vancomycin and piperacillin/tazobactam. Clin Infect Dis. 2017;64(5):666-674.
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3. Navalkele B, Pogue JM, Karino S, et al. Risk of acute kidney injury in patients on concomitant vancomycin and piperacillin-tazobactam compared to those on vancomycin and cefepime. Clin Infect Dis 2017; 64:116–23.
4. Karino S, Kaye KS, Navalkele B, et al. Epidemiology of acute kidney injury among patients receiving concomitant vancomycin and piperacillin-tazobactam: opportunities for antimicrobial stewardship. Antimicrob Agents Chemother 2016; 60:3743–50.
5. Richard R Watkins, Stan Deresinski, Increasing Evidence of the Nephrotoxicity of Piperacillin/Tazobactam and Vancomycin Combination Therapy—What Is the Clinician to Do? Clinical Infectious Diseases, Volume 65, Issue 12, 15 December 2017, Pages 2137–2143, <https://doi.org/10.1093/cid/cix675>