

“Facility Name” Protocol		
Title: Extended Infusion Autosubstitution Piperacillin-tazobactam (Zosyn)	Control No.:	Version: 3
Replaces: v.2 Extended Infusion Autosubstitution Piperacillin-tazobactam (Zosyn)		
Document Owner:		
Reviewers:		
Approvers: Medical Executive Committee (Chairman), Medical Staff P.I. Committee (Chairman) Medical Staff	Date Approved: 05/18/2017	Date Last Reviewed: 05/18/2017

Purpose: To assist in the optimization of pharmacodynamic dosing of piperacillin-tazobactam (Zosyn) based upon minimum inhibitory concentration (MIC) and renal function in ADULT patients.

Supportive Data:

For Beta-lactam antibiotics, in vitro and animal studies indicate that the time that free drug remains above the MIC ($fT > MIC$) predicts bactericidal activity. In vivo data has confirmed that $fT > MIC$ is the pharmacodynamic parameter that is correlated with therapeutic efficacy for various Beta-Lactams. Population pharmacokinetics and Monte Carlo simulation models assist in developing rational Beta-Lactam dosing strategies that optimize the likelihood of attaining bactericidal activity based upon a desired $fT > MIC$ for the range of organisms most likely to be found in clinical practice. Alternative dosing regimens can thus be devised and implemented to potentially optimize patient outcomes and as a secondary benefit, minimize antimicrobial costs.

Equipment:

References:

1. Lodise TP, Lomaestro B, Drusano GL. Piperacillin-tazobactam for Pseudomonas aeruginosa infection: Clinical Implications of an extended-infusion strategy. Clin Infect Dis 2007; 44:357-63.
2. Shea MK, Cheatham SC, Smith DW, et al. Comparative pharmacodynamics of intermittent and prolonged infusions of piperacillin/tazobactam using Monte Carlo simulations and steady-state pharmacokinetic data from hospitalized patients. Ann Pharmacother 2009; 43:1747-54.
3. Patel N, Scheetz HM, Drusano GL, Lodise TP. Identification of optimal renal dosing for traditional and extended infusion piperacillin-tazobactam dosing regimens in hospitalized patients. Antimicrob Agent Chemother 2010; 54:460-5.
4. Mohr JF, Wanger A, Rex JH, Pharmacokinetic/pharmacodynamic modeling can help guide targeted antimicrobial therapy for nosocomial gram-negative infections in critically ill patients. Diagn Microbiol Infect Dis 2004; 48:125-30.
5. Kim A, Sutherland CA, Kuti JL, Nicolau DP: Optimal dosing of piperacillin-tazobactam for the treatment of Pseudomonas aeruginosa infections: prolonged or continuous infusion? Pharmacotherapy 2007; 27:1490-7.

6. Xamplas RC, Itokazu GS, Glowacki RC, et al. Implementation of an extended-infusion piperacillin-tazobactam program at an urban teaching hospital. Am J Health-Syst Pharm 2010; 67:622-8.
7. UpToDate (electronic version). Wolters Kluwer. Available at <http://www.uptodate.com/contents/piperacillin-and-tazobactam-sodium-drug-information> (cited: 04/06/2017).

Procedure:

Pharmacist will automatically convert all prescribed ADULT (greater than 18 years) piperacillin-tazobactam (Zosyn)intermittent regimens to the following equivalent extended infusion regimen. Subsequent doses will also be adjusted based on renal function.

Dosage Conversion between intermittent and extended infusion regimens:		
Creatinine Clearance:	Pseudomonas Dosing:	Extended Infusion Dosing:
Greater than 20 mls/minute:	4.5gm IV q 8 hrs (over 4 hours)	3.375gm IV q 8 hrs (over 4 hrs)
Less than 20 mls/minute	4.5gm IV q 12 hrs (over 4 hours)	3.375gm IV q 12 hrs (over 4 hrs).

EXEMPTIONS for the extended infusion time would be:

1. Pre-op or Intra-op doses.
2. First doses administered within the Emergency Department in which a 4-hour infusion time may not be possible, and the intermittent infusion will be permitted upon the discretion of the physician and/or nursing staff.