

**TITLE: EXTENDED INFUSIONS (PHARMACODYNAMIC DOSING) OF  
PIPERACILLIN/TAZOBACTAM AND MEROPENEM- ADULT GUIDELINES**

**GUIDELINES:**

Based on recommendations from the Subcommittee on Anti-Infective Use and the Formulary and Therapeutics Committee, these guidelines shall be used by prescribers and pharmacy personnel to optimize pharmacodynamic dosing of piperacillin/tazobactam and meropenem and to minimize expenditures associated with the use of these antimicrobials.

**PURPOSE:**

To assist in the optimization of pharmacodynamic dosing of piperacillin/tazobactam and meropenem based upon minimum inhibitory concentration (MIC) and renal function.

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 minimize antimicrobial costs.

**APPLICABILITY:**

NYP/WC and NYP/CU

**PROCEDURE:**

Please reference Tables I – II for dosing and Tables III - IV for intravenous compatibility.

**RESPONSIBILITY:**

Joint Subcommittee on Anti-Infective Use

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**Table I- Piperacillin/Tazobactam (Adult)**

**Dose for known MICs ≤16 mg/L and empiric dosing regimens\***

Maximum Adult Daily Dose	CrCL >20 mL/min	CrCL <20 mL/min, Hemodialysis, and Peritoneal Dialysis	Continuous Renal Replacement Therapy (CRRT)
27 g	4.5 g over 4 hours q8h	4.5 g over 4 hours q12h	4.5 g over 4 hours q8h

\*Extended-infusion dosing of piperacillin/tazobactam optimizes its pharmacodynamic profile against organisms with MICs up to and including 16 mg/L. For infections due to organisms with MICs >16 mg/L, consider an alternative antimicrobial agent.

**Table II- Meropenem (Adult)**

**Dose for known MICs 4 – 16 mg/L in non-lactose fermenting Gram-negatives and mucoid *Pseudomonas aeruginosa***

Maximum Adult Daily Dose	CrCL >50 mL/min	CrCL 30 - 50 mL/min	CrCL 10 - 30 mL/min	CrCL <10 mL/min	Hemodialysis	Peritoneal Dialysis	Continuous Renal Replacement Therapy (CRRT)
6 g	2 g over 3 hours q8h	2 g over 3 hours q12h	500 mg over 30 min q8h	500 mg over 30 min q12h	500 mg over 30 min q12h	500 mg over 30 min q12h	2 g over 3 hours q8h

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**Table III- Piperacillin/tazobactam IV Solutions Compatibility**

Drug	Y-Site Compatibility	Admixture Compatibility
Vasopressin	Compatible	Not tested
Norepinephrine	Compatible	Not tested
Epinephrine	Compatible	Not tested
Phenylephrine	Compatible	Not tested
Dopamine	Compatible	Not tested
Dobutamine	Incompatible	Not tested
Pantoprazole	Incompatible	Not tested
Esomeprazole	Not tested	Not tested
Hydrocortisone	Compatible	Not tested

**Table IV- Meropenem IV Solutions Compatibility**

Drug	Y-Site Compatibility	Admixture Compatibility
Vasopressin	Compatible	Not tested
Norepinephrine	Compatible	Compatible
Epinephrine	Not tested	Not tested
Phenylephrine	Not tested	Not tested
Dopamine	Not tested	Compatible
Dobutamine	Not tested	Compatible
Pantoprazole	Incompatible	Not tested
Esomeprazole	Not tested	Not tested
Hydrocortisone	Not tested	Not tested

**REFERENCES:**

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- 3) Lodise TP, Lomaestro B, Rodvold KA, et al. Pharmacodynamic profiling of piperacillin in the presence of tazobactam in patients through the use of population pharmacokinetic models and Monte Carlo simulation. *Antimicrob Agents Chemother* 2004;48:4718-4724.
- 4) Shea KM, Cheatham SC, Mack MF, et al. Steady-state pharmacokinetics and pharmacodynamics of piperacillin/tazobactam administered by prolonged infusion in hospitalised patients. *Int J Antimicrob Agents* 2009;34:429-433.
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**GUIDELINE DATES:**

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