


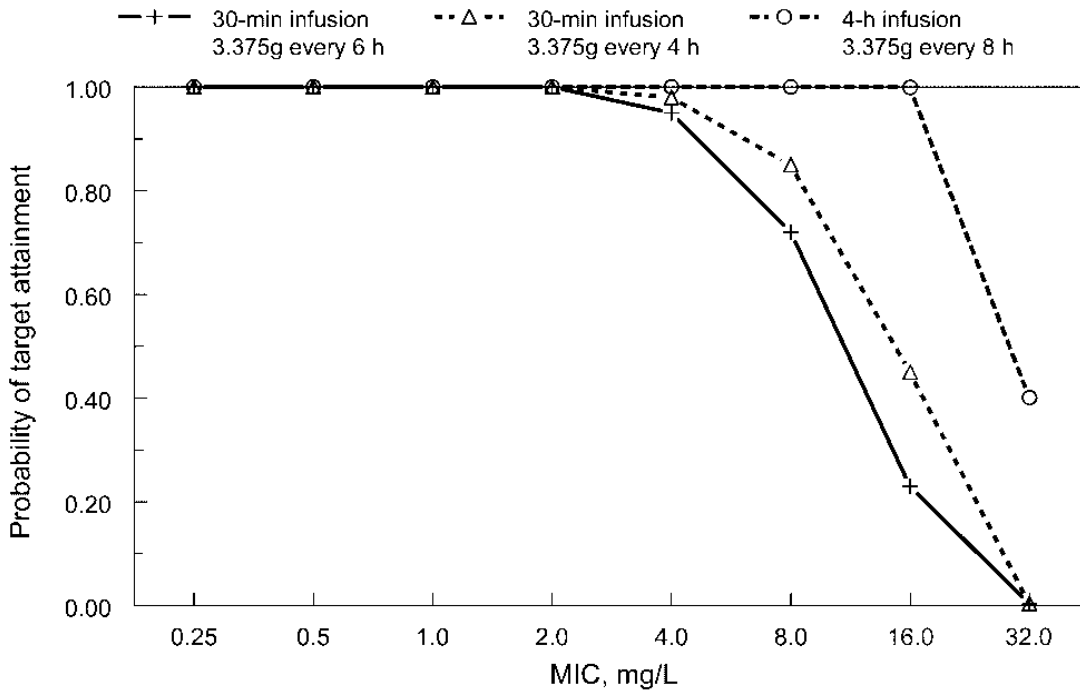
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| <b>Name of Policy:</b> <u>Extended Infusion Piperacillin-Tazobactam</u><br><b>Policy Number:</b> 3364-133-107<br><b>Department:</b> Pharmacy<br><b>Approving Officer:</b> Senior Hospital Administrator<br><b>Responsible Agent:</b> Director of Pharmacy<br><b>Scope:</b> University of Toledo Medical Center | <br><br><b>Effective Date:</b> 2/20/2023<br><b>Initial Effective Date:</b> 4/2013 |
| <input type="checkbox"/> New policy proposal<br><input type="checkbox"/> Major revision of existing policy   | <input checked="" type="checkbox"/> Minor/technical revision of existing policy<br><input type="checkbox"/> Reaffirmation of existing policy                         |

**(A) Policy Statement**

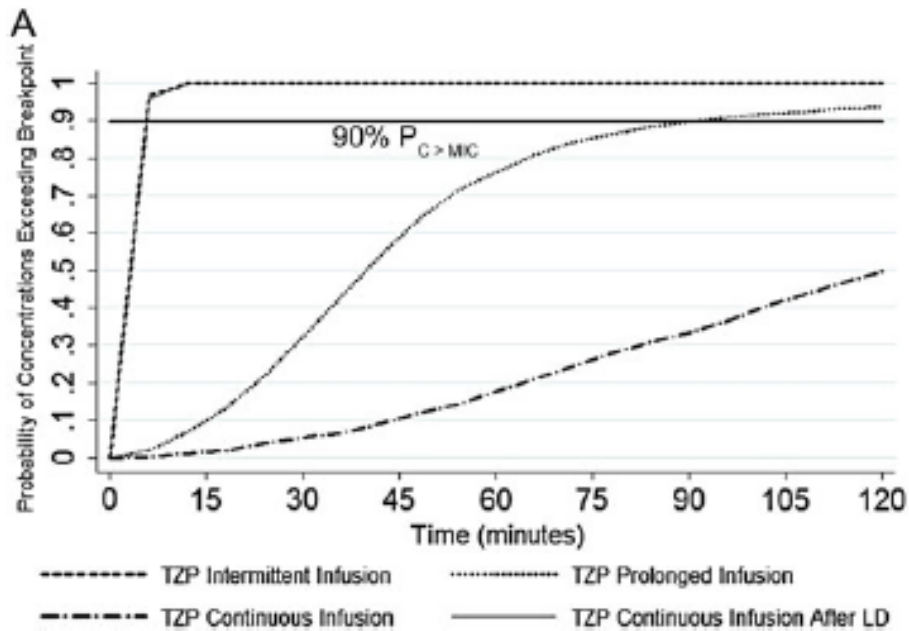
All inpatients prescribed piperacillin-tazobactam (Zosyn) therapy will receive a loading dose followed by an extended infusion regimen according to renal function. Subsequent doses may be infused via traditional 30-minute infusion in special circumstances as outlined below or pursuant to a provider order to change infusion time

**(B) Purpose of Policy**

Administration of piperacillin-tazobactam by extended infusion optimizes the pharmacodynamic properties and bactericidal activity resulting in a potential improvement in patient outcomes<sup>1,2</sup>. The probability of target attainment (50%  $fT > MIC$ ) against *Pseudomonas aeruginosa* isolates according to MIC is depicted below



However, the time by which 90% of patients are expected to exceed the breakpoint (90%  $P_{C > MIC}$ ) is 96 minutes using extended infusion versus 6 minutes using a 30-minute loading dose<sup>3</sup>



**(C) Procedure**

1. All inpatient provider orders for piperacillin-tazobactam will be prescribed as a 4.5 gram loading dose via traditional 30-minute infusion followed by a 3.375-gram dose via extended infusion every 8 or 12 hours based on renal function (see Table 1). This will be facilitated by the computerized order entry system
  - a. Exclusions:
    - i. One-time doses administered to all patients in the emergency department or pre-operatively will be via traditional 30-minute infusion
    - ii. Patients with line access issues may be changed to traditional 30-minute infusion pursuant to a provider order (see Table 2)
      1. When placing an electronic order for piperacillin-tazobactam, providers may indicate in the comments section the need for traditional 30-minute infusions as well as the dose and frequency of traditional 30-minute infusion piperacillin-tazobactam
      2. Alternatively, pharmacy may change administration times of incompatible intravenous medications to coincide with a time in which piperacillin-tazobactam is not being administered
    - iii. Patients requiring continued therapy with 4.5 gram doses will be handled on a case-by-case basis
2. Upon order entry and during profile review, pharmacists will verify patients are receiving the correct dosing regimen of extended infusion piperacillin-tazobactam according to Table 1

**Table 1. Dosing Regimens<sup>3-5</sup>**

| Estimated Creatinine Clearance <sup>a</sup> | Loading Dose <sup>b</sup>          | Maintenance Dose   |
|---|------------------------------------|--|
| > 20 mL/min, CRRT                           | 4.5 gm x 1 infused over 30 minutes | 3.375 gm IV q8h infused over 4 hours<br><b>Start 4 hours after loading dose</b>  |
| ≤ 20 mL/min, IHD, PD                        | 4.5 gm x 1 infused over 30 minutes | 3.375 gm IV q12h infused over 4 hours<br><b>Start 8 hours after loading dose</b> |

CRRT= continuous renal replacement therapy; IHD= intermittent hemodialysis; PD= peritoneal dialysis

<sup>a</sup>Estimated creatinine clearance as calculated by Cockcroft-Gault

<sup>b</sup>No loading dose is required in patients who have previously received piperacillin-tazobactam within the previous 24 hours

**Table 2. Non-Compatible via Y-Site<sup>6</sup>**

|                |              |                  |               |                  |
|----------------|--------------|------------------|---------------|------------------|
| Acyclovir      | Dantrolene   | Ganciclovir      | Levofloxacin  | Phenytoin        |
| Alemtuzumab    | Daunorubicin | Gemcitabine      | Methadone     | Prochlorperazine |
| Amiodarone     | Diltiazem    | Glycopyrrolate   | Midazolam     | Promethazine     |
| Amphotericin B | Dobutamine   | Haloperidol      | Minocycline   | Propranolol      |
| Azithromycin   | Dolasetron   | Hydralazine      | Mitomycin     | Tobramycin       |
| Chlorpromazine | Doxorubicin  | Hydroxyzine      | Mitoxantrone  | Topotecan        |
| Ciprofloxacin  | Doxycycline  | Idarubicin       | Mycophenolate | Tranexamic acid  |
| Cisplatin      | Droperidol   | Insulin, regular | Nalbuphine    | Trastuzumab      |
| Codeine        | Epirubicin   | Irinotecan       | Nicardipine   | Vecuronium       |
| Dacarbazine    | Famotidine   | Labetalol        | Pantoprazole  | Verapamil        |

Note: This list is not comprehensive. See drug reference for additional compatibilities.

There is conflicting data for the compatibility of piperacillin-tazobactam with amikacin, gentamicin, and cisatracurium. Additionally, no information exists on the compatibility of piperacillin-tazobactam and micafungin

Piperacillin-tazobactam and vancomycin are reliably compatible in 0.9% sodium chloride at piperacillin-tazobactam concentrations up to 67.5 mg/mL and vancomycin concentrations up to 5 mg/mL (see Table 3)

**Table 3. Vancomycin and Piperacillin-Tazobactam Concentrations and Compatibility<sup>7</sup>**

| Drug <sup>a,b</sup>     | Dosage                | Diluent | Volume | Concentration               |
|-------------------------|-----------------------|---------|--------|-----------------------------|
| Piperacillin-tazobactam | 4.5gm (4gm-0.5gm)     | NS      | 100 mL | 45mg/mL (40mg-5mg/mL)       |
| Piperacillin-tazobactam | 3.375gm (3gm-0.375gm) | NS      | 100 mL | 33.75mg/mL (30mg-3.75mg/mL) |
| Vancomycin              | 750mg                 | NS      | 250 mL | 3mg/mL                      |
| Vancomycin              | 1gm                   | NS      | 250 mL | 4mg/mL                      |
| Vancomycin              | 1250 mg               | NS      | 250 mL | 5mg/mL                      |
| Vancomycin              | 1500 mg               | NS      | 500 mL | 3mg/mL                      |
| Vancomycin              | 1750 mg               | NS      | 500 mL | 3.5mg/mL                    |
| Vancomycin              | 2gm                   | NS      | 500 mL | 4mg/mL                      |

<sup>a</sup>Vancomycin hydrochloride for injection, APP Pharmaceuticals, Schaumburg, IL

<sup>b</sup>Piperacillin sodium and tazobactam for injection, Hospira or Zosyn for injection, Wyeth Pharmaceuticals, Philadelphia, PA

References:

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2. Roberts J, Kirkpatrick C, Roberts M, Dalley A, Lipman L. First-dose and steady-state population pharmacokinetics and pharmacodynamics of piperacillin by continuous or intermittent dosing in critically ill patients with sepsis. *International Journal of Antimicrobial Agents.* 2010;35:156-163.
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5. Patel N, Scheetz M, Drusano G, Lodise T. Identification of optimal renal dosage adjustments for traditional and extended-infusion piperacillin-tazobactam dosing regimens in hospitalized patients. *Antimicrob Agents and Chemotherapy.* 2010;54(1):460-465.
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7. O'Donnell J, Venkatesan N, Manek M, Rhodes N, Scheetz M. Visual and absorbance analyses of admixtures containing vancomycin and piperacillin-tazobactam at commonly used concentrations. *Am J Health Syst Pharm.* 2016;73(4):241-6.

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| <p><b>Approved by:</b></p><br><p><u>/s/</u> <span style="float: right;"><u>2/17/2023</u></span><br/>         Lindsey Eitniece, PharmD, BCPS, AAHIVP<br/>         Director of Pharmacy<br/> <span style="float: right;">Date</span></p><br><p><u>/s/</u> <span style="float: right;"><u>2/16/2023</u></span><br/>         Russell Smith, Pharm D, MBA, BCPS<br/>         Senior Hospital Administrator<br/> <span style="float: right;">Date</span></p> <p><i>Review/Revision Completed By:</i><br/>         Matt Rico, PharmD, BCIDP</p> | <p><b>Review/Revision Date:</b><br/>         4/1/2017<br/>         10/25/2018<br/>         2/17/2023</p><br><p><b>Next Review Date:</b> 2/1/2026</p> |
| <p><b>Policies Superseded by This Policy:</b></p>  |  |