

IREDELL HEALTH SYSTEM

Zosyn Extended Dosing Interval	
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Antimicrobial Stewardship Committee P&T Committee	Date: 09/2020 Date: 10/2020

Purpose

β -lactams are time-dependent killers; therefore, time above MIC (T>MIC) is the most important determinant of bacterial eradication and clinical response. For penicillins, MIC must be exceeded for ~50% of a dosing interval. Given the short elimination half-life of piperacillin-tazobactam (Zosyn®), traditional dosing strategies using an intermittent 30-minute infusion may result in serum concentrations below the MIC for a prolonged period of time. Pharmacodynamic principles can be used to design antibiotic dosing and administration strategies that optimize antibiotic exposure, and thus, may ameliorate resistance.

Administration of piperacillin-tazobactam by extended-infusion (EI) optimizes the pharmacodynamic properties and bactericidal activity of the drug. Prolonging the infusion to half the dosing interval enhances drug exposure. Studies have shown that extended-infusions (EI) of piperacillin-tazobactam are equally effective as continuous infusions. EI allows for a decreased total daily dose (reduction in drug expenditure) and less nursing administration time while providing a four hour “drug-free” interval for other medications to be administered.

A growing body of literature has looked at utilization of extended infusions of β -lactam antibiotics as a means to increase T>MIC and therefore increase antibiotic exposure. Literature has suggested regimens that utilize 4 hour extended-infusion of piperacillin-tazobactam administered every 8 hours improve outcomes in patients with *Pseudomonas aeruginosa* infections. Lodise et al reported a significant decrease in 14 day mortality and duration of hospitalization among critically ill patients after implementation of piperacillin tazobactam extended-infusion.

Policy

All orders for traditional infusions of piperacillin-tazobactam will be automatically substituted to an EI in adults via the following:

Zosyn 3.375 g IV q8 hours as a 4 hour infusion	CrCl > 20 mL/min
Zosyn 3.375 g IV q12 hours as a 4 hour infusion	CrCl ≤ 20 mL/min or hemodialysis

- Pediatric populations and pre-operative surgical prophylaxis doses will be excluded from extended-infusion dosing.
- Pharmacy will collaborate with nursing to schedule other IV medications during the 4 hour “drug-free” interval when possible.
- Doses of piperacillin-tazobactam given in the ED, PACU, and OR will be administered over 30 minutes. When continued for inpatients, the next dose will be given as an

extended infusion 6 hours after the ED, PACU, or OR dose for creatinine clearance > 20mL/min, or 8 hours after the ED, PACU or OR dose for patients with creatinine clearance ≤ 20mL/min or on hemodialysis.

Procedure

Pharmacy:

1. Pharmacy will automatically convert all orders for piperacillin-tazobactam to an extended infusion strategy as described above.
2. Piperacillin-tazobactam to be given via a four hour extended infusion will be dispensed in a pre-mixed 50 mL bag or ad-mixed in 50 mL of NS (depending on availability of product).
3. The bag will be labeled “Extended Infusion- DO NOT INTERRUPT.”
4. Reschedule incompatible IV meds during the “Zosyn-free” intervals when possible.

Nursing:

1. IV lines should be flushed with 10 mL NS (20 mL in PICC lines) prior to and after the infusion.
2. The bag will be labeled instructing the nurse (Extended Infusion- DO NOT INTERRUPT). Tubing should also be labeled at the proximal end of the line.
3. Important: The antibiotic infusion should not be interrupted once started. If multiple drug orders are present, consult pharmacy for rescheduling of other medications.
4. Many medications are compatible via Y-Site with piperacillin-tazobactam. Do not automatically assume that an additional line or a PICC line is needed solely due to multiple medications ordered. Check compatibility charts.
5. Doses of piperacillin-tazobactam given in the ED, OR and PACU will be administered over 30 minutes.

INITIAL EFFECTIVE DATE: 10/2012

DATES REVISIONS EFFECTIVE: 11/2014, 10/2017, 12/2020

DATES REVIEWED (no changes):

References

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3. Lodise TP Jr., et.al. Piperacillin-tazobactam for *Pseudomonas aeruginosa* infection: Clinical implications of an extended-infusion dosing strategy. *CID* 2007; 44: 357-63.
4. 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. *Antimicrobial Agents and Chemotherapy* 2010; 54: 460-65.
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6. Heinrich LS, Tokumaru S, Clark NM, Garofalo J, Paek J, Grim SA. Development and Implementation of a piperacillin-tazobactam extended infusion guideline. *Journal of Pharmacy Practice* 2011; 24: 571-576.