Prolonged Antibiotic Infusion Pathway

Eligibility

Inclusion Criteria
(if patient has any of these)

- Critical illness
- Infection with multidrug resistant organism (MDRO)
- Febrile neutropenia
- Cystic fibrosis (CF)
- Methicillin sensitive *Staphylococcus aureus* (MSSA) endocarditis
- Obesity (BMI >95% percentile)
- Meningitis

Exclusion Criteria

- Lack of line access
- IV incompatibility

→ Continue intermittent infusion antibiotic administration

Action

Consider Precautions: Due to limited evidence, consider risks and benefits before recommending prolonged beta-lactam in the following:

- ❑ Neonates (< 30 days)
- ❑ Creatinine clearance (CrCl) <20 ml/min/1.73m^2
- ❑ Concurrent dialysis (any type) or renal replacement therapy

Pharmacy Responsibilities

- ❑ Verify compatibility of each IV antimicrobial agent with other concomitantly administered IV medications.
- ❑ Confirm timing for prolonged infusion and coordinate with bedside nurse (e.g., cefepime 2 g IV over 4 hr every 8 hr at 0400, 1200, 2000).
- ❑ Dispense the appropriate antimicrobial infusion solution and concentration with the label stating prolonged infusion.

Nursing Responsibilities

- ❑ Coordinate timing of prolonged infusion dose administration with the MAR and pharmacist.
- ❑ Consult pharmacist to confirm compatibility of the antibiotic with other concomitantly administered IV medications.
- ❑ Administer prolonged infusion therapy over the prescribed duration via smart pump.

Monitoring

- ❑ Monitor urine output and patient labs per physician discretion (CBC with differential, serum creatinine)

Owner: Laura Bio, PharmD & Hayden Schwenk, MD
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Associated Order panel: Prolonged Infusion Beta-Lactam Antibiotics

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Definitions

- **Beta-lactam antibiotics:** Class of antibiotic agents that contain a beta-lactam ring including penicillins, cephalosporins, monobactams, and carbapenems
- **Prolonged infusion:** Lengthening of the standard infusion duration, including:
  - **Extended-infusion (EI):** Dose administered over approximately half of the dosing interval (i.e., over 4 hr for an 8-hr dosing interval)
  - **Continuous infusion:** Dose administered over 22-24 hr (depending on compatibility)
- **Intermittent Infusion:** Short, standard infusion lasting 30 to 60 minutes
- **MIC:** Minimum inhibitory concentration

Background

Beta-lactam antibiotics have time-dependent bactericidal activity relying on optimal duration in which the free drug concentration exceeds the MIC of the bacteria (*f*T>MIC). Prolonged infusion (i.e., extended and continuous infusion) of beta-lactam antibiotics maximizes the duration of antibiotic serum concentration above the bacteria's MIC and therefore can enhance antibiotic activity and improve patient outcomes.[1-3]

Purpose

- ❑ To provide a standard procedure for ordering and administering prolonged infusions of beta-lactam antibiotics
- ❑ To optimize the pharmacokinetics/pharmacodynamics of beta-lactam antibiotics for improved efficacy

	Extended IV infusion (EI)	Continuous IV infusion	CRRT*
Cefepime	LD, then 4 hr later 50 mg/kg over 4 hr every 8 hr (max 2 g/dose)	NA	Same as EI dose
Ceftazidime	LD, then 4 hr later 50 mg/kg over 4 hr every 8 hr (max 2 g/dose)	CF: 150 mg/kg over 21-24 hr every 24 hr (max 12 g/day)	NA
Meropenem	LD, then 4 hr later 20 mg/kg over 3 hr every 8 hr (max 1 g/dose) High dose: LD, then 4 hr later 40 mg/kg over 3 hr every 8 hr (max 2 g/dose)	NA	Same as EI dose
Nafcillin	NA	200 mg/kg, IV over 21-24 hr Every 24 hr (max 12 g/day)	NA
Piperacillin/ tazobactam	≤ 6 years of age: see Housestaff manual > 6 years: LD, then 4 hr later 100 mg/kg over 4 hr q8h (max 4 g/dose) High dose: LD, then 3 hr later 100 mg/kg over 3 hr q6h (max 4 g/dose)	NA	Same as EI dose

First dose of prolonged infusion requires a load dose (LD), followed by the extended or continuous infusion (use the order panel to ensure appropriately shortened dosing interval)

*For CRRT (continuous renal replacement therapy), consider starting EI after 24 hours of standard infusion (30 min.) if no LD

References:

1. Zembles TN, et al. Extended Infusion of Beta-Lactams Is Associated With Improved Outcomes in Pediatric Patients. J Pediatr Pharmacol Ther. 2021;26(2):187-193.
2. Bauer KA, et al. Extended-infusion cefepime reduces mortality in patients with Pseudomonas aeruginosa infections. Antimicrob Agents Chemother. 2013 Jul;57(7):2907-12.
3. Roberts JA, et al.; DALI Study. DALI: defining antibiotic levels in intensive care unit patients: are current β-lactam antibiotic doses sufficient for critically ill patients? Clin Infect Dis. 2014 Apr;58(8):1072-83.

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