Office of Origin: Department of Pharmaceutical Services, Antimicrobial Stewardship Program, Department of Nursing

I. PURPOSE

To develop an extended infusion (EI) protocol for inpatients receiving piperacillin/tazobactam with the goal of decreasing the dose of antibiotic needed to achieve equivalent or superior therapeutic target compared to standard short infusion (SI).

II. BACKGROUND/JUSTIFICATION

Pharmacokinetic/pharmacodynamic studies have demonstrated that EI dosing of piperacillin/tazobactam achieves target time above concentration goals for adequate empirical and definitive therapy of bacterial infections, including treatment of susceptible Pseudomonas.

III. REFERENCES

1. Pharmacist Prescribing Authority: 6.09.09 Medication Management: Pharmacist Prescribing Authority
2. Department of Nursing Medication Administration procedure
3. Department of Nursing IV Pump – Alaris© Medley with Guardrails procedure
4. IDMP Website: idmp.ucsf.edu


IV. POLICY

a. Inpatients being treated with piperacillin/tazobactam will receive EI unless the patient meets the exceptions stated below.

b. Exclusion Criteria (These patients should receive piperacillin/tazobactam SI unless otherwise noted):
   i. Pediatric patients admitted to Benioff Children’s Hospital
   ii. Patients with creatinine clearance of < 20ml/min, not on continuous renal replacement therapy (CRRT)
iii. Patients on intermittent hemodialysis (iHD). Note that patients on continuous renal replacement therapy should get EI dosing unless meeting other exclusion criteria.

iv. Patients with infection or colonization with gram-negative bacteria intermediate or resistant to piperacillin/tazobactam within the last 60 days
   a) Consult with Infectious Diseases or Antimicrobial Stewardship for consideration of alternative therapies.

v. Patients with cystic fibrosis

vi. Patients stationed in the operating room, or peri-procedural areas.

vii. Patients with insufficient intravenous access

V. PROCEDURES
   a. Definitions
      i. Extended intravenous infusion (EI): Infusion over 4 hours
      ii. Short intravenous infusion (SI): Infusion over 30 minutes
      iii. Continuous renal replacement therapy (CRRT)
      iv. Intermittent Hemodialysis (iHD)

   b. Responsibilities
      i. Provider ordering
         a) Determine whether the patient is eligible for EI. For patients meeting exclusion criteria discussed in section IV, subsection b, piperacillin/tazobactam should be ordered as a SI with appropriate dosing selected for renal function. All other patients should get EI dosing.

         b) For patients ordered to receive EI, determine when the last dose of piperacillin/tazobactam was administered.

            i) Patients who have not received a dose of piperacillin/tazobactam SI within 6 hours or EI started within 10 hours: piperacillin/tazobactam should be ordered as EI with loading dose. Please consult with a clinical pharmacist in the case of a patient previously on EI piperacillin/tazobactam with last dose started 10-14 hours ago.

            ii) Patients who have received a dose of piperacillin/tazobactam SI within 6 hours or EI started within 10 hours: piperacillin/tazobactam should be ordered as EI without loading dose.
ii. Pharmacist Verification
   a) Review each order for appropriateness, including but not limited to:
      i) Allergies
      ii) Indication
      iii) Site of infection
      iv) Suspected pathogens
      v) Drug compatibilities
      vi) Timing of administration
   b) Replace SI orders with EI orders, unless patient meets exclusion criteria outlined in Section IV, Subsection b.
   c) Replace EI orders with SI orders, as outlined in Section VI for patients meeting exclusion criteria outlined in Section IV, Subsection b.
   d) Assess need for loading dose of piperacillin/tazobactam based on last piperacillin/tazobactam administration time.
      i) Patients who have not received a dose of piperacillin/tazobactam SI within 6 hours or EI started within 10 hours: order a piperacillin/tazobactam loading dose as outlined in Section VI, if not already ordered by the provider. If the last dose of piperacillin/tazobactam EI was started 10-14 hours ago, please use best judgement based on renal function, indication, and clinical status when assessing need for loading dose. If assistance is needed, consult the Antimicrobial Stewardship Program pharmacist.
      ii) Patients who have received a dose of piperacillin/tazobactam SI within 6 hours or EI started within 10 hours: no loading dose is needed. Cancel the loading dose if ordered by the provider.
   e) Adjust timing of piperacillin/tazobactam, depending on when the last dose, if any, was administered.
   f) Adjust timing of piperacillin/tazobactam with incompatible IV medications, if applicable. See Appendix I.

iii. Nursing Administration
   a) Administer medication following the Medication Administration and IV pump Alaris Medley with Guardrails nursing procedures.
b) To administer a STAT IV medication that is incompatible with piperacillin/tazobactam, stop EI piperacillin/tazobactam, flush the line, and administer the STAT IV medication. Then, resume EI piperacillin/tazobactam.

VI. DOSING RECOMMENDATIONS

### Extended Infusion (4 hour infusion) in 100ml 0.9% NaCl

<table>
<thead>
<tr>
<th>Loading Dose (LD), if indicated*</th>
<th>CrCl &gt; 20 ml/min or CRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance Dose (starting 4 hrs after loading dose, if indicated)</td>
<td>4.5 gm IV over 4 hr q8h</td>
</tr>
</tbody>
</table>

* Only give a LD if there has not been a SI dose within 6 hours or an EI dose started within 10 hours

### Short infusion (30-minute infusion) in 100 ml 0.9% NaCl

<table>
<thead>
<tr>
<th>General infections</th>
<th>CrCl ≥ 50 ml/min</th>
<th>CrCl 10-50 ml/min</th>
<th>CrCl &lt; 10 ml/min</th>
<th>Dialysis (HD or CRRT)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.375 gm IV Q6h</td>
<td>3.375 gm IV Q6-8h</td>
<td>2.25 gm IV Q8h</td>
<td>HD: 2.25 gm IVq8h</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CRRT: 4.5 gm IV Q8h or 3.375 gm IV Q6h</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Documented/suspected Pseudomonas infections</th>
<th>CrCl &gt; 20 ml/min: 4.5 gm IV Q6h</th>
<th>CrCl &lt; 20 ml/min: 2.25 gm IV Q8h</th>
<th>HD: 2.25 gm IVq8h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CRRT: 4.5 gm IV Q8h or 3.375 gm IV Q6h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## APPENDIX I: Common Y-site IV incompatibilities

| Known incompatible agents | Acyclovir | Amiodarone HCL | Amphotericin B (cholesteryl and conventional colloidal) | Caspofungin | Chlorpromazine | Ciprofloxacin | Cisplatin | Daunorubicin | Decarbazine | Dobutamine | Doxorubicin | Doxyccycline | Droperidol | Diltiazem | Famotidine | Ganciclovir | Gemcitabine | Haloperidol | Hydralazine | Hydroxyzine | Idarubicin | Insulin regular | Levofoxacin | Mitomycin | Mitoxantrone | Minocycline | Nalbuphine | Phenytoin | Prochlorperazine | Promethazine | Promethazine | Tobramycin |
|---------------------------|-----------|----------------|----------------------------------------------------------|-------------|----------------|--------------|------------|--------------|-------------|------------|-------------|---------------|-------------|------------|-------------|-------------|-------------|-------------|--------------|-------------|-------------|--------------|-------------|--------------|-------------|----------------|-------------|-------------|-------------|-------------|-------------|-------------|----------------|-------------|-------------|-------------|
|                           |           |                |                                                          |             |                |              |            |              |             |            |             |                |             |            |             |             |             |             |              |             |             |              |             |              |             |                |             |             |             |             |             |             |                |             |             |             |
| Variable compatibility    | Azithromycin | Cisatracurium | Gentamicin \(^b\) | Pantoprazole | Ganciclovir | Gemcitabine | Haloperidol | Hydralazine | Hydroxyzine | Idarubicin | Insulin regular | Levofoxacin | Mitomycin | Mitoxantrone | Minocycline | Nalbuphine | Phenytoin | Prochlorperazine | Promethazine | Promethazine | Tobramycin |

\(^a\) List is not comprehensive. Refer to Micromedex or LexiComp for more compatibility information.

\(^b\) Avoid mixing aminoglycosides & penicillin in the same bag and avoid infusing concurrently through same line.