Piperacillin/tazobactam (Zosyn®)

Restriction Status

- JHH: RESTRICTED — ID approval required unless part of an orderset
- Bayview: RESTRICTED — ID approval required on all non ICU floors; Doses of 4.5 g require ID approval in all ICUs

Activity

- Piperacillin/tazobactam is a β-lactam and β-lactamase inhibitor combination antibiotic.
- It has activity against a wide range of Gram-negative bacteria including Enterobacteriaceae (including those that produce ESBLs), *P. aeruginosa*, and *Achromobacter* spp.
- Its Gram-positive activity is limited to *Streptococcus* spp., *E. faecalis*, and MSSA.
- It does NOT have activity against MRSA or *Stenotrophomonas* spp.
- It is also active against wide range of anaerobes.

Acceptable Use

- Empiric treatment for severe infections in patients where broad spectrum coverage is needed, including *Pseudomonas* spp.
- Non-severe infections (e.g., UTIs) caused by ESBL-producing organisms with adequate source control
- Neutropenic fever
- Polymicrobial infections when coverage for *P. aeruginosa*, Gram-positives (e.g., *E. faecalis*, MSSA), and anaerobes is needed
- Urosepsis with nephrostomy tube

Unacceptable Use

- Empiric treatment for non-severe infections in patients without risk for *Pseudomonas* spp. (e.g., CAP)
- Severe infections caused by ESBL-producing *E. coli*, *Proteus* spp., *Klebsiella* spp. (e.g., Ceftriaxone MIC > 1) due to higher failure rates.
- Treatment for meningitis or endocarditis
- In combination with other broad spectrum β-lactams such as Meropenem and Cefepime

Adult Dosing

Formulation

Components of each Piperacillin/tazobactam dose:

- 2.25 g = 2 g of Piperacillin and 0.25 g of Tazobactam
- 3.375 g = 3 g of Piperacillin and 0.375 g of Tazobactam
- 4.5 g = 4 g of Piperacillin and 0.5 g of Tazobactam

Standard Dosing

- Usual dose: 3.375 g IV Q6H
- Suspected or confirmed *Pseudomonas* spp. or suspected or confirmed non-severe ESBL infections: 4.5 g IV Q6H
- Cystic fibrosis: 3.375 g IV Q4H
- Neutropenic fever: 4.5 g IV Q6H

Renal Dosing
<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>3.375 g IV Q6H</th>
<th>3.375 g IV Q4H</th>
<th>4.5 g IV Q6H</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 40</td>
<td>Normal dose</td>
<td>Normal dose</td>
<td>Normal dose</td>
</tr>
<tr>
<td>20−40</td>
<td>2.25 g IV Q6H</td>
<td>3.375 g IV Q6H</td>
<td>3.375 g IV Q6H</td>
</tr>
<tr>
<td>&lt; 20</td>
<td>2.25 g IV Q8H</td>
<td>2.25 g IV Q6H</td>
<td>2.25 g IV Q6H</td>
</tr>
<tr>
<td>HD†</td>
<td>2.25 g IV Q12H</td>
<td>2.25 g IV Q8H</td>
<td>2.25 g IV Q8H</td>
</tr>
</tbody>
</table>

† If patient on intermittent hemodialysis (iHD) schedule administration so that patient receives daily dose immediately AFTER HD.

- For assistance with dosage adjustments for patients receiving CVVHD or CVVHDF, please call pharmacy.

**Hepatic Dosing**
- No dosage adjustment needed

**Monitoring**

**Safety**
- Weekly CBC, BUN, SCr

**Lab Interactions**
- False-positive galactomannan results have been reported with earlier preparations of Piperacillin/tazobactam. Recent data suggests that this is no longer a concern.

**Adverse Effects**
- Hypersensitivity reactions (rash)
- Interstitial nephritis
- Biliary sludge
- Pancytopenia with prolonged use and/or higher doses

**References**

   - **Comment**: Spanish study suggesting that piperacillin/tazobactam was equally effective as carbapenems for treatment of non-severe bacteremia (e.g., biliary or urinary source) caused by ESBL-producing organism. Piperacillin/tazobactam dose used in majority of patients in this study was 4.5 g q6h.

   - **Comment**: Hopkins data suggesting mortality benefit when carbapenems were used to treat severe bacteremia caused by ESBL-producing organisms compared to piperacillin/tazobactam.