Stanford Health Care Aminoglycoside Dosing Guideline

I. DETERMINING DOSE AND CREATININE CLEARANCE:

1. Use of total body weight (TBW) in underweight and non-obese patients is widely accepted. Use of ideal body weight (IBW) for determining the mg/kg/dose may also be considered. For obese patients (total body weight > 20% over ideal body weight), dosage requirement may best be estimated using an adjusted body weight (ABW) of: IBW + 0.4 (TBW - IBW).^1

   IBW (male) = 50 kg + (2.3 x height in inches > 60 inches)
   IBW (female) = 45 kg + (2.3 x height inches > 60 inches)

2. Calculate creatinine clearance with the Cockcroft-Gault equation using an ideal body weight (IBW) or an adjusted body weight (ABW) if the patient is obese

   \[
   \text{CrCL (mL/min)} = \frac{(140 - \text{age}) \times \text{IBW} \times (x 0.85 \text{ for females})}{\text{SCr} \times 72}
   \]

II. AMINOGLYCOSIDE DOSING STRATEGIES

A. Gram negative infections

1. High-dose Extended-Interval Therapy

   **Rationale:**
   - Aminoglycoside bactericidal activity is generally regarded as concentration dependent.^2,3 The higher the peak/MIC ratio, the greater the rate and extent of bacterial kill. The pharmacodynamic goal is to maximize drug concentration at the site of infection. Optimum bactericidal activity for the aminoglycosides is achieved when the exposure concentration is approximately 8 to 10 times the MIC. Existing data also supports area under the plasma concentration-time curve (AUC) / MIC ratio as an indicator of bacterial killing and efficacy. The AUC:MIC targets are for efficacy range from AUC/MIC ratios of 30-50 in non-critically ill immunocompetent patients and upwards of 80-100 for critically ill patients with infections of high-bacterial burden.^4
   - Aminoglycosides exhibit a post-antibiotic effect (PAE).^2,5-7 PAE ranges of 0.5 to 8-hours have been reported. Factors influencing the PAE include: height of the preceding AMG peak, in-vivo > in-vitro, shortened by neutropenia, and extended in the presents of beta-lactams
   - Saturable aminoglycosides uptake in renal tubule cell and inner ear. This suggests that higher peaks do not result in greater risk of toxicity. A single dose of aminoglycoside results in significantly lower renal cortical tissue concentration compared to the same total dose administered through a continuous infusion or in divided doses.^8.\textsuperscript{9,10} Modeling data suggests that thrice-daily administration is associated with nephrotoxicity that occurs more rapidly, with greater intensity, and for longer duration, as compared to once-daily aminoglycoside.\textsuperscript{11} Clinical data and experience suggests that high-dose extended interval may be less nephrotoxicity compared to traditional regimens.\textsuperscript{12,13}

   The **Hartford Nomogram** method utilizes high-dose, once daily dosing to optimize the peak/MIC ratio in most clinical situations by administering a dose of 7mg/kg of either gentamicin or tobramycin. The **Urban & Craig Nomogram** is another method of extended-interval therapy utilizing 5 mg/kg of gentamicin or tobramycin in patients without renal dysfunction. For patients with **cystic fibrosis exacerbation** the Cystic Fibrosis consensus guidelines recommend extended interval dosing with 10 mg/kg once daily.

   **Exclusion Criteria:**
   - Renal insufficiency (CrCl <30 mL/min or rapidly declining renal function)
   - Pregnancy
   - Synergy for gram-positive infections
   - Ascites
   - Burns (>20%)

2. Conventional / Traditional Dosing

   Tradition dosing includes reduced doses and more frequent administration of aminoglycosides using pharmacokinetic parameters to determine dose and frequency to achieve target peak and trough values.

   **Indication:**
   - Treatment of gram-negative infections and **NOT** a candidate for high-dose extended interval dosing therapy (see exclusion criteria above)

B. Gram positive-synergy

Synergy dosing is a low dose of aminoglycoside in conjunction with an antimicrobial agent that exhibits activity against the cell wall of Gram-positive bacteria (i.e. beta-lactams, glycopeptides) for the treatment of Gram-positive infections

C. Non-tuberculosis mycobacterium (NTM)

Treatment of NTM infections include combination therapy of either macrolides, clarithromycin, azithromycin, ethambutol, rifamycin and possibly an aminoglycoside. The decision to add an aminoglycoside depends on multiple factors including the extensiveness of disease, drug-refractory/resistant profile, and drug tolerance.
Dosing Methods by Indication

Indication for Aminoglycoside

Gram Negative Infection

Are there any contraindications for High-Dose Extended-Interval Dosing?
- Dialysis
- Burn > 20% BSA
- Significant Ascites
- Pregnancy

YES

Gentamicin/Tobramycin 1.7mg/kg q8h

NO

High-Dose Extended-Interval (Appendix A)

Streptococcus virdans/bovis

Gentamicin 3 mg/kg q24h

Staphylococcus spp

Gentamicin 1 mg/kg q8h OR 1.5 mg/kg q12h

Enterococcus spp

Gentamicin 1 mg/kg q8h OR 1.5 mg/kg q12h

Non-tuberculosis Mycobacterial Infection (Appendix D)

Amikacin 10-15 mg/kg q24h OR Amikacin 10-25 mg/kg 3 times weekly

Gentamicin

1 mg/kg q8h

OR

1.5 mg/kg q12h

CONVENTIONAL/ TRADITIONAL DOSING (Appendix B)

Gentamicin/Tobramycin 1.7mg/kg q8h

Hartford Nomogram

Gentamicin/Tobramycin 7 mg/kg q24h

Consider in the following scenarios (e.g.):
- Multi-drug resistant pseudomonal infections w/elevated MICs (MIC >2)
- Severe sepsis/septic shock

(Appendix A1)

Urban-Craig Nomogram

Gentamicin/Tobramycin 5 mg/kg q24h

Consider in the following scenarios (e.g.):
- Complicated urinary tract infections/pyelonephritis
- Surgical prophylaxis
- Gynecologic, GYN/ONC infections
- Orthopedic open-fracture

(Appendix A2)

CF exacerbation

Tobramycin 7 – 10 mg/kg q24h

(Appendix A3)

Consult ID Pharmacists for other indications not listed above (e.g. Nocardiosis, Listeriosis)

Are there any contraindications for High-Dose Extended-Interval Dosing?
- Dialysis
- Burn > 20% BSA
- Significant Ascites
- Pregnancy

YES

NO

• Dialysis
• Burn > 20% BSA
• Significant Ascites
• Pregnancy

YES

NO
Appendix A: High-Dose Extended-Interval Nomograms (Gram-negative infections)

Appendix A1: Hartford Nomogram

**Initial Dose:**
- **7 mg/kg using actual body weight** (Nomogram was developed and validated with actual body weight)
- If obese, use adjusted body weight if obese: IBW + (0.4 [TBW – IBW])
- The dose of 7 mg/kg is expected to achieve a $C_{max}$ level of ~20 mcg/mL

<table>
<thead>
<tr>
<th>CrCL (mL/min)</th>
<th>Gentamicin / Tobramycin</th>
<th>Amikacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 mL/min</td>
<td>7 mg/kg Q24H</td>
<td>15 mg/kg Q24H</td>
</tr>
<tr>
<td>40 – 59 mL/min</td>
<td>7 mg/kg Q36H</td>
<td>15 mg/kg Q36H</td>
</tr>
<tr>
<td>30 – 39 mL/min</td>
<td>7 mg/kg Q48H</td>
<td>15 mg/kg Q48H</td>
</tr>
<tr>
<td>20 – 29 mL/min</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>&lt; 20 mL/min</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>CRRT</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

**Monitoring:**

**Initial Monitoring**
- Random level drawn ~10-hours after the first dose
- Use nomogram to confirm/modify dosage interval
- **Hartford nomogram is only applicable for 7 mg/kg** – plotting doses lower or higher than 7 mg/kg may under or overestimate clearance
  - **Gentamicin/tobramycin (7 mg/kg/dose):**
    - Plot level on graph
  - **Amikacin (15 mg/kg/dose):**
    - Divide level in half, then plot on graph

**Follow up trough level testing**
- **Trough monitoring** (30-60 minutes prior to dose) should be considered in patients demonstrating acute changes in renal function or suspicion of extended interval failure
- **Maintenance random levels** should be monitored at least once weekly
- **If duration of therapy is anticipated to be > 2 weeks,** audiometry should be considered

![Nomogram Graph](image-url)
Appendix A2: Urban & Craig Nomogram

**Initial Dosing:**

- Gentamicin/Tobramycin 5 mg/kg IV Q24H based on actual body weight
  - If obese, use adjusted body weight if obese IBW + (0.4 [TBW – IBW])

<table>
<thead>
<tr>
<th>CrCL (mL/min)</th>
<th>Gentamicin / Tobramycin</th>
<th>Amikacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 mL/min</td>
<td>5 mg/kg Q24H</td>
<td>15 mg/kg Q24H</td>
</tr>
<tr>
<td>40 – 59 mL/min</td>
<td>5 mg/kg Q36H</td>
<td>15 mg/kg Q36H</td>
</tr>
<tr>
<td>20 – 39 mL/min</td>
<td>5 mg/kg Q48H</td>
<td>15 mg/kg Q48H</td>
</tr>
<tr>
<td>&lt; 20 mL/min</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>CRRT</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

**Monitoring:**

**Initial Monitoring**
- Single level drawn 10-hours after the first dose.
- Use nomogram to confirm/modify dosage interval.
- Only applicable for 5 mg/kg – plotting doses lower or higher than 7 mg/kg may under or overestimate clearance
- Gentamicin/Tobramycin 5 mg/kg/dose
- Amikacin 15 mg/kg/dose (divide level in half, then plot on graph)

**Follow up monitoring:**
- Trough monitoring (30-60 minutes prior to dose) should be considered in patients demonstrating acute changes in renal function or suspicion of extended interval failure
- Maintenance random levels should be monitored at least once weekly
- If duration of therapy is anticipated to be > 2 weeks, audiometry should be considered
Appendix A3: Cystic Fibrosis Dosing

Initial Dosing:

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Tobramycin</th>
<th>Amikacin</th>
<th>Timing of Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 mL/min</td>
<td>7 – 10 mg/kg Q24H</td>
<td>20 mg/kg Q24H</td>
<td>Peak 30 min after 1st dose</td>
</tr>
<tr>
<td>40 – 59 mL/min</td>
<td>7 – 10 mg/kg Q36H</td>
<td>20 mg/kg Q36H</td>
<td>Random level (7 mg/kg Q24H dosing): Random Level 10-hours after first dose</td>
</tr>
<tr>
<td>30 – 39 mL/min</td>
<td>7 – 10 mg/kg Q48H</td>
<td>20 mg/kg Q48H</td>
<td></td>
</tr>
<tr>
<td>20 – 29 mL/min</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Trough 60 min before 2nd or 3rd dose (peak/trough should be from the same dose). Time the paired peak/trough after the same dose.</td>
</tr>
<tr>
<td>&lt; 20 mL/min</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td></td>
</tr>
</tbody>
</table>

CRRT Not recommended Not recommended

Monitoring:

<table>
<thead>
<tr>
<th>Goal Levels</th>
<th>Target Peak</th>
<th>Target Trough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin/Tobramycin</td>
<td>20 – 30 mcg/mL</td>
<td>&lt; 1 – 2 mcg/mL</td>
</tr>
<tr>
<td>Amikacin</td>
<td>40 – 60 mcg/mL</td>
<td>&lt; 4 – 8 mcg/mL</td>
</tr>
</tbody>
</table>

Appendix B: Conventional / Traditional Dosing (Gram-negative infections)

Initial Dosing:

<table>
<thead>
<tr>
<th>CrCL (mL/min)</th>
<th>Gentamicin / Tobramycin</th>
<th>Amikacin</th>
<th>Timing of Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60 mL/min</td>
<td>1.7 mg/kg Q8H</td>
<td>7.5 mg/kg Q12H or 5 mg/kg Q8H</td>
<td>Peaks 30-min after 3rd dose</td>
</tr>
<tr>
<td>40 – 59 mL/min</td>
<td>1.7 mg/kg Q12H</td>
<td>5 – 7.5 mg/kg Q12H</td>
<td>Troughs Before 4th dose</td>
</tr>
<tr>
<td>30 – 39 mL/min</td>
<td>1.7 mg/kg Q24H</td>
<td>5 – 7.5 mg/kg Q24H</td>
<td></td>
</tr>
<tr>
<td>20 – 29 mL/min</td>
<td>1.7 mg/kg Q24H</td>
<td>5 – 7.5 mg/kg Q24H</td>
<td></td>
</tr>
<tr>
<td>&lt; 20 mL/min; AKI</td>
<td>2 mg/kg load, then dose by level</td>
<td>5 mg/kg load, then dose by level</td>
<td>30-min after 1st dose</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2 mg/kg load, then 1.5 mg/kg post-HD: Redose for 4-hr post-HD level Cp&lt;1 mg/L or pre-HD</td>
<td>5 – 7.5 mg/kg post-HD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cp &lt; 1 mg/L (mild UTI)</td>
<td>5 – 7.5 mg/kg post-HD</td>
<td>30-min after 1st dose</td>
</tr>
<tr>
<td></td>
<td>Cp &lt; 2–3 mg/L (moderate-severe UTI)</td>
<td>5 – 7.5 mg/kg post-HD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cp &lt; 3–5 mg/L (severe GNR infection)</td>
<td>5 – 7.5 mg/kg post-HD</td>
<td>4-hr post-HD level Cp &lt; 1 mg/mL -- OR -- pre-HD levels based on indication</td>
</tr>
<tr>
<td>CRRT</td>
<td>1.5 – 2.5 mg/kg Q24-48H</td>
<td>10 mg/kg load, then 7.5 mg/kg Q24-48H</td>
<td>30-min after 2nd dose</td>
</tr>
</tbody>
</table>

Monitoring:

<table>
<thead>
<tr>
<th>Goal Levels</th>
<th>Indication</th>
<th>Target Peak</th>
<th>Target Trough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin/Tobramycin</td>
<td>Life-threatening infection</td>
<td>8 – 10 mcg/mL</td>
<td>&lt; 1 – 2 mcg/mL</td>
</tr>
<tr>
<td></td>
<td>Serious Infections</td>
<td>6 – 8 mcg/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urinary tract infections</td>
<td>4 – 6 mcg/mL</td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Life-threatening infection</td>
<td>25 – 30 mcg/mL</td>
<td>&lt; 4 – 8 mcg/mL</td>
</tr>
<tr>
<td></td>
<td>Serious Infections</td>
<td>20 – 25 mcg/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urinary tract infections</td>
<td>15 – 20 mcg/mL</td>
<td></td>
</tr>
</tbody>
</table>
Appendix C: Gram-Positive Synergy Dosing

**Initial Dosing:**

<table>
<thead>
<tr>
<th>CrCL (mL/min)</th>
<th>Synergy Dosing (Gentamicin/Tobramycin)</th>
<th>Timing of Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>1 mg/kg Q8H*</td>
<td>Peaks 30 minutes after 3rd dose</td>
</tr>
<tr>
<td>40-59</td>
<td>1 mg/kg Q12H</td>
<td>Troughs Before 4th dose</td>
</tr>
<tr>
<td>30-39</td>
<td>1 mg/kg Q24H</td>
<td>Before 3rd dose</td>
</tr>
<tr>
<td>20-29</td>
<td>1 mg/kg Q24H</td>
<td>Before 2nd dose</td>
</tr>
<tr>
<td>&lt;20; AKI</td>
<td>1 mg/kg x 1 dose; redose when Cp &lt; 1 mcg/mL</td>
<td>Before 2nd dose, redose when Cp &lt; 1 mcg/mL</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>1 mg/kg q48–72H; Redose for pre-HD or post-HD Cp &lt;1mcg/mL</td>
<td>Before 2nd dose, redose when Cp &lt; 1 mcg/mL</td>
</tr>
<tr>
<td>CRRT</td>
<td>1 mg/kg Q24H, then by level</td>
<td>Before 3rd dose</td>
</tr>
</tbody>
</table>

*Alternative dosing only for CrCl > 60 mL/min:
- **Gentamicin 3 mg/kg q24h** for treatment of endocarditis with Streptococi, *Streptococcus gallolyticus* (bovis), *Streptococcus viridans*
- **Gentamicin 1.5 mg/kg q12h** for treatment of endocarditis with *Staphylococci; Enterococcus spp* (strains susceptible to PCN and gentamicin) endocarditis

**Monitoring:**

<table>
<thead>
<tr>
<th>Goal Levels</th>
<th>Target Peak</th>
<th>Target Trough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin/Tobramycin</td>
<td>3 – 4 mcg/mL**</td>
<td>&lt; 1 mcg/mL</td>
</tr>
</tbody>
</table>

**Target Peak levels not applicable for alternative regimens of Gentamicin 3mg/kg q24h or 1.5 mg/kg q12h.**

Appendix D: Non-TB Mycobacterial Infections

**Initial Dosing:**

<table>
<thead>
<tr>
<th>CrCL (mL/min)</th>
<th>Amikacin Daily Regimen</th>
<th>Amikacin Thrice Weekly Regimen</th>
<th>Timing of Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 mL/min</td>
<td>10 – 15 mg/kg Q24H</td>
<td>10 – 25 mg/kg TIW</td>
<td>Peaks 30 minutes after 2nd dose completion (or 60 minutes after starting infusion)</td>
</tr>
<tr>
<td>Age &gt; 50 years old: 10 mg/kg Q24H (max single dose of 500 mg)</td>
<td>Age &gt; 50 years old: 10 mg/kg TIW (max single dose of 500 mg)</td>
<td>Troughs 30 – 60 minutes after 2nd dose</td>
<td></td>
</tr>
<tr>
<td>40 – 59 mL/min</td>
<td>10 – 15 mg/kg Q36H</td>
<td></td>
<td>Maintenance Monitoring</td>
</tr>
<tr>
<td>Alt: 10 mg/kg q24h</td>
<td></td>
<td>Weekly peaks/troughs for prolonged duration of therapy</td>
<td></td>
</tr>
<tr>
<td>30 – 39 mL/min</td>
<td>10 – 15 mg/kg Q48H</td>
<td></td>
<td>Acute renal changes</td>
</tr>
<tr>
<td>20 – 29 mL/min</td>
<td>Dose by level</td>
<td>Dose by level</td>
<td>Changes in dosing regimen</td>
</tr>
<tr>
<td>&lt; 20 mL/min</td>
<td>Dose by level</td>
<td>Dose by level</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Dose by level</td>
<td>Dose by level</td>
<td></td>
</tr>
<tr>
<td>CRRT</td>
<td>Dose by level</td>
<td>Dose by level</td>
<td></td>
</tr>
</tbody>
</table>

**Monitoring:**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Peaks***</th>
<th>Target Trough</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 – 15 mg/kg Q24H</td>
<td><em>Expected levels: 25 – 40 mcg/mL</em></td>
<td>&lt; 4 mcg/mL</td>
</tr>
<tr>
<td>10 – 25 mg/kg three times weekly</td>
<td>- May consider goal peaks of 35 – 45 mcg/mL as tolerability permits</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Some expert opinions recommend a target peak of 20 – 30 mcg/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*Expected levels with 25 mg/kg: 65 – 85 mcg/mL</td>
<td>&lt; 4 mcg/mL</td>
</tr>
</tbody>
</table>

**Note:** There is no established PK/PD target for optimal microbiologic and clinical outcome. The above peak values are typically expected and therefore have been suggested TDM targets by national guidelines. The goal trough is to ensure drug clearance and minimize accumulation/toxicity.
### Aminoglycoside Pharmacokinetic Parameters

<table>
<thead>
<tr>
<th>PK parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability (F)</td>
<td>- Water soluble</td>
</tr>
<tr>
<td></td>
<td>- Poorly lipid soluble</td>
</tr>
<tr>
<td></td>
<td>- Poor oral absorption</td>
</tr>
<tr>
<td>Volume of Distribution</td>
<td>0.25 L/kg (0.1 – 0.5 L/kg)</td>
</tr>
<tr>
<td>Fraction unbound in plasma</td>
<td>&gt; 0.95</td>
</tr>
</tbody>
</table>

#### Clearance
- Normal renal function: Same as CrCL
- Functionally anephric: 0.0043 L/kg/hr
- Hemodialysis: 1.8 L/hr

<table>
<thead>
<tr>
<th>t ½</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal renal function</td>
<td>2 – 3 hours</td>
</tr>
<tr>
<td>Functionally anephric</td>
<td>30 – 60 hours</td>
</tr>
</tbody>
</table>

### Initial Dosing

1. **Determine CrCL using Cockcroft-Gault**
   
   \[ CrCL (\text{mL/min}) = \frac{(140 - \text{age}) \times \text{IBW} \times 0.85}{\text{SCr} \times 72} \]

2. **Estimate elimination rate constant (Ke) based on PK kinetics**
   
   \[ Ke = (0.003 \times \text{CrCl}) + 0.01 \]

3. **Estimate half-life (t ½)**
   
   \[ t \frac{1}{2} = \frac{0.693}{Ke} \]

4. **Calculate Volume of distribution (Vd) using ABW or AdjBW**
   
   - Gentamicin/Tobramycin: 0.25 L/kg
   - Amikacin: 0.3 L/kg

5. **Infusion time**
   
   - Gentamicin/Tobramycin: 30 minutes
   - Amikacin: 30 minutes; 60 minutes if doses > 15 mg/kg

6. **Estimated dosing interval based on goal levels**
   
   \[ T = \frac{\left( \ln \left( \frac{C_{\text{max}}}{C_{\text{min}}} \right) \right)}{Ke} + t_i \]
   
   OR
   
   \[ \text{Estimated (T)} = 3 \times t \frac{1}{2} \]

7. **Maintenance dose (MD):**
   
   \[ MD = \frac{\left[ (K_e) \times (VD) \times (t_i) \times (C_{\text{peak desired}}) \times (1 - e^{-KeT}) \right]}{\left[ (1 - e^{-KeT}) \right]} \]
   
   OR
   
   \[ MD = (C_{\text{peak desired}}) \times VD \]

### Abbreviations

- IBW = ideal body weight
- ABW = actual body weight
- DBW = dosing body weight
- kel = elimination rate constant
- Vd = volume of distribution
- τ = dosing interval
- t = time of infusion
- t_{before} = time between blood draw and start of infusion
- t_{end} = time from end of infusion to blood draw
- t_{1/2} = half-life
- C_{max} = peak serum level at steady-state
- C_{min} = trough serum level at steady-state
- SCr = serum creatinine
## Individualized Dose Revisions

1. **Determine elimination rate constant**  
   Use levels within the same dosing interval  
   
   \[ K (hr^{-1}) = \frac{\text{Ln peak/trough}}{\Delta \text{time between levels}} \]  
   OR  
   \[ k = \frac{\text{Ln (Cmax/Cmin)}}{\tau - (t_{end} + t_{before})} \]

2. **Determine actual Cmax**  
   (if level not drawn at correct time; 1 hour after the start or 30 minutes after completion of infusion)  
   \[ C_{\text{max, actual}} = \frac{C_{\text{max}}}{e^{k(t_{end})}} \]

3. **Determine half-life**  
   \[ t_\frac{1}{2} = \frac{0.693}{k} \]  
   Dosing interval for traditional dosing method = ~ 3-4 times the half-life

4. **Time to achieve goal trough level**  
   Time to clearance = \( \frac{\text{Ln (actual trough/ desired trough)}}{K_e} \)

5. **Estimate dosing interval**  
   \[ \tau = \left[ \frac{\text{Ln (Cmax/Cmin)}}{K} \right] + ti \]  
   OR  
   Estimated \( \tau = 3 \times t_\frac{1}{2} \)

6. **Determine Vd**  
   \( t_1 = \text{time from beginning infusion to Cpeak} \)  
   \[ Vd (L) = \frac{\text{Dose}}{C_{\text{max, actual}} (1 - e^{K(t_{end})})} \]  
   OR  
   \[ Vd (L) = \left[ \frac{(\text{Dose}/C_{\text{peak}})}{(1 - e^{Kt_1})} \right] \times e^{Kt_1} \]

7. **New maintenance dose**  
   \( ti = \text{infusion time} \)  
   \( \tau = \text{interval} \)  
   \[ MD = \frac{\left[ (K_e) \times (Vd) \times (ti) \times (C_{\text{peak, desired}}) \times (1 - e^{-K\tau}) \right]}{\left[ (1 - e^{-K\tau}) \right]} \]  
   OR  
   \[ MD = \text{(goal peak Cmax)} \times Vd \]
References


Document Information

A. Original Author/Date
   Emily Mui, PharmD: 05/2012

B. Gatekeeper
   Pharmacy
   Stanford Antimicrobial Safety & Sustainability Program (SASS Program)

C. Review and Renewal Requirement
   This document will be reviewed every three years and as required by change of law or practice

D. Revision/Review History
   Emily Mui, PharmD: 05/2013, 08/2017, 05/2018
   Lina Meng, PharmD: 05/2018

E. Approvals
   Approved by Antimicrobial Subcommittee: 05/2012, 05/2013, 08/2017, 05/2018
   Approved by P&T Committee: 05/2012, 05/2013, 09/2017