# Stanford Hospital & Clinics Antibiotic Dosing Reference Guide 2011

This document is also located on the SHC Intranet (http://portal.stanfordmed.org/depts/pharmacy) P&T Approved April 15, 2011

**Formulas for dosing weights**: Ideal body weight IBW (male) = 50 kg + (2.3 x height in inches > 60 inches)· IBW (female) = 45 kg + (2.3 x height inches > 60 inches)
Adjusted BW (kg) = IBW + 0.4 (TBW – IBW)

| Drug | CrCl >50 mL/min | CrCl 10–50 mL/min | CrCl <10 mL/min | Intermittent Hemodialysis (IHD) | CRRT |
|---|---|---|---|---|---|
| **Acyclovir (IV)**[1,4,5, 6,7,8] **(Use ideal BW for obese)** | HSV:5 mg/kg q8h<br>HSV encephalitis/zoster:<br>10 mg/kg q8h | Same dose<br>CrCl 25–50: q12h<br>CrCl 10 – 25: q24h | HSV:<br>2.5 mg q24h<br>HSVencephalitis/zoster<br>5 mg/kg q24h | HSV: 2.5mg/kg q24h<br>HSV encephalitis/zoster:<br>5mg/kg q24h<br>Dose after HD on HD days | HSV: 5 – 7.5 mg/kg q24h<br>HSV encephalitis/zoster:<br>7.5–10 mg/kg q12h |
| **Acyclovir (PO)**[1,5] | HSV mucocutaneous:<br>200 mg q4h (or 5x daily)<br>VZV, HSV zoster:<br>800 mg q4h (or 5x/day) | Same dose q8h | Same dose q12h | Same dose q12h | n/a |
| **Ambisome**[1]**(Ampho BLiposomal)** | 3 –6 mg/kg/day | No change (caution: nephrotoxic) | No change | No change | No change |
| **Amikacin**[1,2,3, 7] **(Use ideal or adjusted BW for obese)**<br>**See appendix for complete guidelines** | CrCl >60: 5 - 7.5 mg/kg q8h; Once daily dosing: 15–20 mg/kg q24h<br>CrCl 40– 60: 5 – 7.5 mg/kg q12h; 15–20 mg/kg q36h<br>CrCl 20–40: 5 – 7.5 mg/kg q24h; 15–20 mg/kg q48h<br>CrCl < 20: 5 mg/kg load, then by level<br>**Timing of levels**: Draw trough 30 min prior to 4th dose. Draw peak 30 min after infusion ends<br>**Once daily dosing**: goal peak 35–60; goal trough <4. Consult Hartford Nomogram<br>**Conventional dosing**: goal peak 25–35 for serious infections, 15–20 for UTI<br>goal trough: <5-8 | | | 5 – 7.5mg/kg post HD only<br>consult pharmacist | 10 mg/kg load,<br>then 7.5mg/kg q24-48h<br>consult pharmacist |
| **Ampicillin (IV)**[1,3,4,6] | 1 – 2 gm q4 – 6h<br>Meningitis/endocarditis:<br>2 gm q4h | same dose q6 – 12h<br>Meningitis/endocarditis:<br>2gm q6h | same dose q12h<br>Meningitis/endocarditis:<br>2gm q12h | 1gmq12h<br>Meningitis/endocarditis:<br>2gm q12h | 1gm q6 –8h<br>Meningitis/endocarditis: 2gm q6h |
| **Ampicillin/sulbactam**[1,2,4, 6,7] **(SHC Restriction)** | 3 gm q6h | CrCl <50: 3gm q8h<br>CrCl <30: 3gm q12h | CrCl <15<br>3gm q24h | 3 gm q12–24h<br>Dose after HD on HD days | 3gm q6 –8h |
| **Azithromycin (IV/PO)**[1] | 500 mg q24h | No change | No change | No change | No change |
| **Aztreonam**[1,2, 6] **Severe**: pseudomonas, meningitis | 1 – 2 gm q8h<br>Severe: 2gm q6–8h | CrCl 10 – 30: 1gm q8h<br>Severe: 1gm q6 – 8h | 500 mg q8h<br>Severe: 500 mg q6 – 8h | 1–2gmLD, then 500 mg q12h<br>Severe: 1–2gm LD, then 500 mg q8h | 1gm q8h or 2 gm q12h |
| **Caspofungin**[1] **(Hepatic adjustment)** | 70 mg x1, then 50 mg q24h<br>Consider 70 mg x 1, then 35mg q24h if severe hepatic dysfunction (Child–Pugh score >7);<br>70 mg q24h if on phenytoin, rifampin, other strong enzyme inducers | | | No change | No change |
| **Cefazolin**[1,2, 5, 6,7, 8] | UTI/mild: 1 gm q8h<br>General: 2 gm q8h | UTI/mild: 1 gm q12h<br>General: 2 gm q12h | 1 gm q24h | 1 gm q24h<br>Dose after HD on HD days | 2 gm q12h |
| **Cefepime**[1,4, 5, 6, 7] **(SHC Interchange)** **Severe**: endocarditis/CF febrile neutropenia/ pneumonia/meningitis/ pseudomonas | CrCl >60: General: 2 gm q12h or 1gm q6h; Severe: 2 gm q8h<br>CrCl 30 –60: General: 2 gm q24h or 1 gm q12h; Severe: 2 gm q12h<br>CrCl < 30: General: 1gm q24h; Severe: 2 gm q24h | | 0.5 gm q24h<br>Severe infections:<br>1 gm q24h | 0.5 gm q24h<br>Severe: 1 gm q24h<br>Give post HD on HD days | 1gm q8h<br>Severe infections:<br>2 gm q12h |
| **Ceftriaxone**[1, 5, 9] | 1 – 2 gm q24h<br>Endocarditis, osteomyelitis: 2 gm q24h<br>Meningitis, *E. faecalis* endocarditis: 2 gm q12h | | No change | No Change<br>Dose after HD on HD days | No Change |
| **Ciprofloxacin(IV/PO)**[1,2, 5, 6, 8] | General infections: CrCl >50: 400 mg IV q12h, 500 mg PO q12h; CrCl 30 – 50: same; CrCl < 30: 400 mg IV q24h, 500 mg PO q24h<br>Pseudomonas, severe: CrCl >50: 400 mg IV q8h, 750 mg PO q12h; CrCl 30 – 50: 400 mg IV q8 – 12h, 500 mg PO q12h; CrCl < 30: 400 mg IV q24h, 500 mg PO q24h | | | 400 mg IV q24h<br>500 mg PO q24h<br>Give post HD on HD days | 400 mg IV q12h<br>500 mg PO q12h |
| **Clindamycin**[1,2](caution in severe hepatic disease) | 600– 900 mg IV q8h<br>150 – 450 mg PO q6h | No change | No change | No change | No change |
| **Colistin**[1,5,6] **(Use ideal BW in obese)** | 1.25 – 2.5mg/kg q12h | $S_{cr}$ 1.3 – 1.5:<br>1.25 - 1.9 mg/kg q12h<br>$S_{cr}$ 1.6 – 2.5:<br>2.5 mg/kg q24h | $S_{cr}$ 2.6–4:<br>1.5 mg/kg q24h | 1.5 mg/kg q24h | 2.5mg/kg q12–24h |
| **Daptomycin**[1, 10, 11, 21] **(Use adjusted BW in obese)** **(SHC Restriction)** | Skin/Soft tissue:4 mg/kg q24h<br>Endocarditis/Bacteremia:<br>6 – 8 mg/kg q24h | (Calculate CrCl using IBW)<br>CrCl < 30:<br>Same dose q48h | Same dose q48h | Same dose q48h<br>Give post HD on HD days | 4 –8mg/kg q48h |
| **Doxycycline (IV/PO)**[1] | 100 mg q12h | No change | No change | No change | No change |
| **Ertapenem**[1] | 1 gm q24h | CrCl <30:500 mg q24h | 500 mg q24h | 500 mg q24h<br>Give post HD on HD days | 1 gm q24h |
| **Ethambutol (PO)**[1,7] | 15 – 25 mg/kg q24h | 15 – 25 mg/kg q24 – 36h | 15 – 25 mg/kg q48h | 15 – 25 mg/kg post HD only | 15 – 25 mg/kg q24 – 36h |
| **Fluconazole(IV/PO)**[1,5,6, 8] Load **800 mg** for candidemia | 200 –400 mg q24h<br>Severe/CNS infections:<br>up to 800 mg q24h | 100 – 200 mg (50% of normal dose) q24h | 50–100 mg (25% of normal dose) q24h | 200 - 400 mg post HD only | 400mg q24h<br>(800 mg q24h for less susceptible organisms) |
| **Foscarnet**[1] | **Please see Lexi-comp or Micromedex for renal dosing table. Note that dosing is by CrCl per kg (ml/min/kg)**<br>CrCl/kg > 1.4: CMV *Induction treatment:* 60 mg/kg q8h **or** 90 mg/kg q12h x 14-21 days | | | | |
| **Ganciclovir**[1, 6] Consider loading dose of **5mg/kg** for all patients | CMV: Induction (I): CrCl >70*: 5 mg/kg q12h; CrCl >50: 2.5 mg/kg q12h; CrCl >25: 2.5 mg/kg q24h; CrCl >10: 1.25 mg/kg q24h; CrCl <10: 1.25 mg/kg 3x/wk<br>Maintenance (M): CrCl >70*: 5 mg/kg q24h; CrCl >50: 2.5 mg/kg q24h; CrCl >25: 1.25 mg/kg q24h; CrCl >10: 0.625 mg/kg q24h; CrCl <10: 0.625 mg/kg 3x/wk<br>*Manufacturer's CrCl cutoffs. **Please refer to BMT protocols if applicable** | | | LD 5mg/kg, then<br>I: 1.25 mg/kg post HD only<br>M:0.625 mg/kg post HD only | LD 5mg/kg, then<br>I: 2.5 mg/kg q12–24h<br>M:1.25 –2.5 mg/kg q24h |
| **Gentamicin**[6] **(SHC interchange to tobramycin. Exception: gram positive synergy)**<br>**See appendix for complete guidelines** | **Gram positive synergy**: CrCl >60: 1mg/kg q8h*; CrCl 40–59: 1mg/kg q12h; CrCl 20–39: 1mg/kg q24h; CrCl <20: 1mg/kg load, then by level; HD: 1mg/kg load, then 1mg/kg post HD only; CRRT: 1mg/kg q12h, then per level<br>**Timing of levels**: Draw trough 30 min prior to 4th dose. Draw peak 30 min after infusion ends (4th dose). (For CrCl <60, check levels sooner than 4th dose) In HD, check trough before each HD session, and peak 30 minutes after each dose.<br>**Goal levels**: For synergy,goal peak 3–5mg/L (3-4 if using IDSA endocarditis guidelines). Goal trough <1 mg/L<br>* Streptococci, *Streptococcus bovis*, *Strep. viridans* endocarditis: optional dosing 3mg/kg q24h for CrCl > 60 | | | | |
| **Imipenem/Cilastatin**[1,2, 6] **(Nonformulary)** | 500 mg q6h | 500 mg q8h | 250– 500 mg q12h | 250 – 500 mg q12h<br>Dose after HD on HD days | 500 mg q8h<br>Severe: 500 mg q6h |
| **Isoniazid**[1] | 300 mg q24h | No change | No change | No change<br>Dose after HD on HD days | No change |

| Drug | CrCl >50 mL/min | CrCl 10–50 mL/min | CrCl <10 mL/min | Intermittent Hemodialysis (IHD) | CRRT |
|---|---|---|---|---|---|
| **Levofloxacin(IV/PO)**[1,2, 5, 6, 8] | General: 250 – 500 mg q24h<br>Pseudomonas/CAP: 750 mg q24h | CrCl 20–50: 250 – 500 mg q48h<br>750 mg q48h | CrCl < 20: 500 mg x1, then 250 mg q48h<br>750 mg x1, then 500 mg q48h | See CrCl < 20 ml/min Dose after HD on HD days | 500 mg q48h<br>Pseudomonas/CAP: 750 mg LD, then 500 mg q24h or 750 mg q48h |
| **Linezolid(IV/PO)**[1,4] **(SHC Restriction)** | 600 mg q12h | No change | No change | No change. Dose after HD on HD days | No change |
| **Meropenem**[1,2, 6, 8, 18] **(SHC Restriction)** **Consider extended infusion (3 hours) or more frequent dosing intervals for pseudomonas or resistant pathogens** | General: CrCl >50: 1 gm q8h or extended infusion 3 hr<br>Severe/CF/CNS: 2 gm q8h | CrCl 26–50: 1 gm q12h or 0.5gm q6h<br>2 gm q12h | CrCl 10–25: 0.5gm q8 – 12h<br>1 gm q12h or 0.5gm q8h | CrCl <10: 0.5gm q12 – 24h<br>0.5gmq12 – 24h | 500 mg q24h Give post HD on HD days<br>Severe/CF/CNS: 1gm q24h Give post HD on HD days | 1 gm q12h or 500 mg q6h<br>Severe/CF/CNS: 2g q12h |
| **Moxifloxacin**[1] | 400 mgIV/PO q24h | No change | No change | No change | No change |
| **Metronidazole(IV/PO)**[1] | 500 mg q6 – 8h | No change | (Can consider 500 mg q12h in long term use or severe hepatic disease) | 500 mg q8h | 500 mg q6 – 8h |
| **Nafcillin**[1] | 2 gm q4h<br>Mild infections: 1gm q4h | No change | No change | No change | No change |
| **Oseltamivir (PO)**[1,2, 15,16,17] | Prophylaxis: CrCl ≥ 30: 75mg q24h; CrCl < 30: 75mg q48h<br>Treatment: 75mg BID; 75mg q24h<br>Treatment (severe/ICU): 150 mg BID; 150 mg q24h | | | Treatment/ prophylaxis: 30 mg<br>Severe/ICU: 60 mg<br>Give after every **other** HD session | Prophylaxis: 75mg q24h<br>Treatment: 75mg BID<br>Severe/ICU: 150 mg BID |
| **Penicillin G (IV)**[1, 5, 6] | 2 – 4 mu q4h | 2– 3mu (75% of dose) q4h | 1– 2 mu (25-50% of dose) q6h | 4mu x1, then 1 – 2 mu q6h | 4mu x1, then 2 – 3 mu q6h |
| **Piperacillin/tazobactam**[1,2,4, 5, 6, 8] | General: CrCl >40: 3.375gm q6h; CrCl 20–40: 2.25gm q6h; CrCl <20: 2.25 gm q8h<br>Pseudomonas/ nosocomial PNA/ severe: 4.5 gm q6h; 3.375gm q6h; 2.25 gm q6h<br>Extended infusion for CrCl > 20: 3.375 gm q8h over 4h | | | 2.25gm q12h<br>Pseudomonas/PNA/ severe infections: 2.25gm q8h | 3.375 gm q6h or Extended infusion 3.375 gm q8h (infused over 4 h) |
| **Posaconazole (PO)**[1,2, 22] **(SHC Restriction)** | Treatment: 200 mg q6h or 400 mg q12h | No change. Posaconazole levels shown to have great degree of interpatient variability. Many clinicians would recommend blood levels to assess efficacy. Consider drawing a trough 4 - 7 days after initiating dose | | | |
| **Pyrazinamide (PO)**[1, 5, 12] **(Use ideal BW)** Round to nearest tablet size | 20 – 25mg/kg IBW q24h (max 2000 mg/day) | CrCl < 30: 25 – 35 mg/kg IBW 3 times per week | | 25 –30 mg/kg IBW after HD only | No data |
| **Rifampin(IV/PO)**[1, 13, 14] | TB: 600 mg q24h<br>Endocarditis: 300 mg q8h | No change | No change | No change | No change |
| **Tobramycin**[20] **(Use ideal or adjusted BW for obese)** **See appendix for complete guidelines** | CrCl >60: 1.7 mg/kg q8h –or– 7mg/kg q24h (once-daily dosing*)<br>CrCl 40–59: 1.7 mg/kg q12h<br>CrCl 20–39: 1.7 mg/kg q24h<br>CrCl <20: 2 mg/kg loading dose, then per level<br>HD: 2 mg/kg loading dose, then 1.5 – 2 mg/kg post HD<br>CRRT: 1.5 - 2 mg/kg q24 - 48h, consult pharmacist<br>**Goal levels:** **Goal peak (4–8mg/L), and trough (<1-2mg/L) for treatment.** ***certain qualifications for once–daily dosing**<br>**Timing of levels:** Draw trough 30 min prior to 4th dose. Draw peak 30 minutes after infusion ends (4th dose). (For CrCL <20, may check levels sooner than 4th dose) For once-daily dosing, draw a single random level 8 to 12 hours after dose given adjustments are made based on a published **Hartford nomogram**. For HD, draw trough pre-HD, and peak 30 min after end of each infusion | | | | |
| **Trimethoprim (TMP)/ Sulfamethoxazole**[1, 5, 6] **(Dose by ideal or adjusted BW in obese)** SS = 80 mg TMP = 10 ml po soln DS =160 mg TMP = 20ml po soln | 5 – 10 mg/kg/day TMP divided q6 – 8h<br>PCP/Stenotrophomonas: 15 – 20 mg/kg/day TMP divided q6-8h | CrCl < 30: 2.5 – 5 mg/kg/day TMP divided q8 – 12h<br>PCP/Stenotrophomonas: 7.5 – 10 mg/kg/day TMP divided q8 –12h | | 2.5 – 5 mg/kg TMP q24h*<br>PCP/ Stenotrophomonas: 7.5 –10 mg/kg TMP q24h*<br>*Give after HD on HD days | 5 – 10 mg/kg/day TMP divided q12h<br>PCP/ Stenotrophomonas: 10 –15mg/kg/day TMP divided q12h |
| **Valganciclovir(PO)**[1] **Please refer to transplant protocols if applicable** | CrCl > 60: Induction (14-21 days): 900 mg q12h; Maintenance/ ppx: 900 mg q24h<br>CrCl 40 – 59: 450 mg q12h; 450 mg q24h<br>CrCl 25 – 39: 450 mg q24h; 450 mg q48h<br>CrCl 10 – 24: 450 mg q48h; 450 mg twice/week<br>CrCl < 10, IHD, CRRT: Not recommended, use ganciclovir | | | | |
| **Vancomycin**[6, 19, 21] **(Use actual body weight)** **Consider loading dose of 20–25mg/kg (max 2gm)** for severe infections and ICU | CrCl >50: 15 – 20 mg/kg q8 – 12h<br>CrCl 30–49: 15 – 20 mg/kg q24h<br>CrCl 15–29: 10 – 15 mg/kg q24h<br>CrCl <15: 10 – 15 mg/kg q24 – 48h<br>**Goal levels:** **Goal trough 10–15 mcg/ml (cellulitis, skin/soft tissue infections)** **Goal trough 15–20 mcg/ml (pneumonia, bacteremia, endocarditis, osteomyelitis)**<br>**Timing of levels:** Draw trough< 30 minutes before 4th dose of new regimen. When SCr acutely rises, hold dose, restart when level <15 - 20<br>**See appendix for complete guidelines** | | | 20 – 25mg/kg LD, then redose with 10 – 15mg/kg post dialysis when level <15 – 20 | 20 – 25mg/kg LD, then 10 – 15mg/kg q24h<br>Draw level prior to 3rddose. Adjust to levels |
| **Voriconazole (IV/PO)**[1,22] **(SHC Restriction)** | 6 mg/kg IV q12h x 2, then 4 mg/kg IV q12h<br>400 mg PO q12h x 2, then 200 mg PO q12h | Caution with IV: accumulation of IV vehicle cyclodextran occurs. Consider PO unless benefits justify risks of IV use. Levels shown to have great degree of interpatient variability. Many clinicians would recommend blood levels to assess efficacy. Consider drawing a trough 4 - 7 days after new dose | | | |

**Abbreviations**: SCr = serum creatinine LD = loading dose; MU= million units; PNA = pneumonia; HD = hemodialysis; CAP = community acquired pneumonia; CRRT = continuous renal replacement therapy; TMP = trimethoprim; PCP: pneumocystis jiroveci pneumonia TB = tuberculosis; UF = ultrafiltration

**CRRT dosing**: doses listed are for CVVHDFand CVVHD modalities, which are the most common modes at SHC. Note that these are generally higher than doses used in CVVH.

All SHC formulary Restrictions/Interchange program descriptions can be accessed using Lexi-Comp and the intranet under pharmacy policies (intranet > Departments > Pharmacy)

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# Stanford Hospital & Clinics Vancomycin Dosing Guidelines

Vancomycin is a tricyclic Glycopeptide antibiotic that exhibits bactericidal activity by preventing the synthesis and assembly of a growing bacterial cell wall, altering the permeability of the bacterial cytoplasmic membrane, and selectively inhibiting bacterial RNA synthesis. Vancomycin is considered to be a concentration-independent or time-dependent killer of bacteria.

**A. Determine creatinine clearance and dose**

a) Determine the dose with total body weight (TBW)
b) 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 (TBW >20% over IBW)

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

IBW (male) = 50 kg + (2.3 x height in inches > 60 inches)
IBW (female) = 45 kg + (2.3 x height inches > 60 inches)
ABW (kg) = IBW + 0.4 (TBW – IBW)

**B. Initial Empiric Dosing**

**Loading Dose:** Consider a loading dose of 20-25mg/kg (max 2gm) for severe infections and ICU patients

| Creatinine Clearance (mL/min) | Dose Total body weight (TBW) | Interval |
|---|---|---|
| **> 50** | 15-20 mg/kg | Q8-12H |
| **30-49** | 15-20 mg/kg | Q12-24H |
| **15-29** | 10-15 mg/kg | Q24H |
| **<15** | 10-15 mg/kg | Q24 – 48H |
| **Hemodialysis** | Load: 20-25 mg/kg x 1<br>Maintenance: 10-15 mg/kg | Post-dialysis when levels <15mg/L or <20 mg/L in severe infections (i.e. meningitis, pneumonia) |
| **CRRT** | Load: 20-25 mg/kg x 1<br>Maintenance: 10-15 mg/kg | Q24H |

**C. Administration**

| Vancomycin Dose | Infusion Rate |
|---|---|
| 500 mg | 60 minutes |
| 1000 mg | 60 minutes |
| 1250 mg | 90 minutes |
| 1500 mg | 90 minutes |

Central line only: Up to 1gm in 100 mL
Peripheral line: Dilute drug in 250 ml

Red man syndrome may occur if the infusion is too rapid. It is not an allergic reaction, but may be characterized by hypotension and/or a maculopapular rash appearing on the face, neck, trunk, and/or upper extremities. If this should occur, slow the infusion rate to over $1^1/_2$ to 2 hours and increase the dilution volume. Reactions are often treated with antihistamines and steroids.

**D. Therapeutic Drug Monitoring**

1. Clinical situations to obtain serum trough concentrations
   - Serious or life-threatening infections
   - Patients with rapidly changing renal function
   - Concomitant administration of nephrotoxic medication (i.e. aminoglycosides, amphotericin B)
   - Patients on intermittent or continuous dialysis
   - Patients requiring higher than usual doses of vancomycin (>20 mg/kg/dose)
   - Altered volume of distribution (i.e. Morbidly obese patients)
   - Treating organisms with higher MICs
   - Patients receiving prolonged course of therapy

2. Timing of serum trough levels
   - Trough levels should be obtained within 30 minutes before the 4$^{th}$ dose of a new regimen
   - For q24h and q48h regimens, consider drawing levels prior to 3$^{rd}$ or 2$^{nd}$ dose respectively
   - Recommend trough levels >10 mcg/mL to avoid microbial resistance
   - When SCr acutely rises, hold dose and draw level. Restart therapy when level <15 - 20

3. Dialysis
   - CRRT: obtain level within 30 minutes prior to 3$^{rd}$ or 4$^{th}$ dose
   - Intermittent hemodialysis (IHD): obtain levels daily before dialysis or consider waiting >4 hours after dialysis to avoid rebound effect
   - Dosing assumes that HD is high flux and removes ~20% of vancomycin per 3 hour session

4. Goal trough levels
   - 10–15 mcg/ml (cellulitis, skin/soft tissue infections)
   - 15–20 mcg/ml (pneumonia, bacteremia, endocarditis, osteomyelitis)

# Stanford Hospital & Clinics Aminoglycoside Dosing Guidelines

Aminoglycosides are concentration dependent antibiotics, meaning that as aminoglycoside concentration increases, the rate and extent of bacterial killing increases. Optimum bactericidal activity for the aminoglycosides is achieved when the exposure concentration is approximately 8 to 10 times the MIC.

**Determining dose and creatinine clearance**

a) Use of ideal body weight (IBW) for determining the mg/kg/dose appears to be more accurate than dosing on the basis of total body weight (TBW). In morbid obesity, dosage requirement may best be estimated using an adjusted body weight (ABW) of: IBW + 0.4 (TBW - IBW)

Obese patients:
Obese is defined as a Total body weight (TBW) > 20% over Ideal body weight (IBW)

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

b) 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

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

**Extended-Interval Therapy (Once daily dosing)**

Hartford Nomogram
The method of once-daily dosing intends to optimize the peak/MIC ratio in the majority of clinical situations by administering a dose of 7mg/kg of either gentamicin or tobramycin. Similar to that of conventional regimens, once-daily protocols also require modification for patients with renal dysfunction in order to minimize drug accumulation. Due to high peak concentrations obtained and the drug-free period at the end of the dosing interval, it is usually not necessary to draw standard peak and trough samples, rather a single random blood sample is obtained between 6 to 14 hours after the start of the aminoglycoside infusion. This concentration is used to determine the dosing interval based on a nomogram for once-daily dosing.

Non-Hartford Nomogram
The second method of extended-interval therapy utilizes a 5mg/kg gentamicin or tobramycin dose in patients without renal dysfunction. If dosage adjustment is required to compensate for impaired renal function, the dose and/or dosing interval may be modified to optimize therapy and minimize drug accumulation.

Exclusion Criteria for Extended Interval Therapy:

- Renal insufficiency (CrCL <30 mL/min or rapidly declining renal function)
- Dialysis
- Pregnancy
- Synergy for gram-positive infections
- Ascites
- Burns (>20%)

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

**Gram positive-synergy Dosing**
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

**Gentamicin & Tobramycin Initial Empiric Dosing**

| CrCL (mL/min) | Once daily dosing* | Traditional | Synergy** |
|---|---|---|---|
| **> 60** | 7mg/kg Q24H | 1.7mg/kg Q8H | 1mg/kg Q8H |
| **40-59** | 7mg/kg Q36H | 1.7mg/kg Q12H | 1mg/kg Q12H |
| **20-39** | 7mg/kg Q48H | 1.7mg/kg Q24H | 1mg/kg Q24H |
| **<20** | Not recommended | 2mg/kg load, then dose by level | 1mg/kg load, then dose by level |
| **Hemodialysis** | Not recommended | 2mg/kg load, then 1.5-2mg/kg post-HD | 1mg/kg load, then 1mg/kg post-HD |
| **CRRT** | Not recommended | 1.5-2.5mg/kg Q24-48H | 1mg/kg Q12H |

*See Hartford nomogram for monitoring of once-daily dosing regimens
**Alternative for synergy: 3mg/kg Q24H for Streptococci and *Streptococcus bovis* endocarditis

**Amikacin Initial Empiric Dosing**

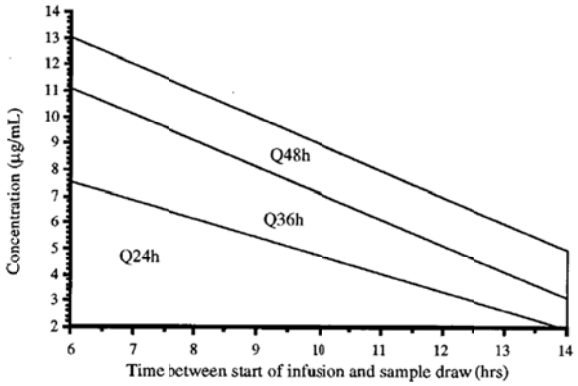
| CrCL (mL/min) | Once daily dosing* | Traditional |
|---|---|---|
| **> 60** | 15mg/kg Q24H | 5-7.5mg/kg Q8H |
| **40-59** | 15mg/kg Q36H | 5-7.5mg/kg Q12H |
| **20-39** | 15mg/kg Q48H | 5-7.5mg/kg Q24H |
| **<20** | Not recommended | 5mg/kg load, then dose by level |
| **Hemodialysis** | Not recommended | 5-7.5mg/kg post-HD |
| **CRRT** | Not recommended | 10 mg/kg load, then 7.5mg/kg Q24-48H |

* See Hartford nomogram for monitoring of once-daily dosing regimens- divide level by half then plot on graph

**Monitoring**

**High Dose Extended Interval (Hartford Nomogram- for once-daily dosing)**

A. Initial level testing: Single level drawn 8-12 hours after the first dose
- Gentamicin/tobramycin: Plot level on graph
- Amikacin: Divide level in half, then plot on graph




B. Follow up trough level testing- for traditional and synergy dosing regimens
- Trough monitoring (30-60 minutes prior to next dose) should be considered in patients demonstrating acute changes in renal function or suspicion of extended interval failure
- Maintenance trough levels should be monitored at least once weekly

**Traditional Regimens**

| | Q8H | Q12H | Q24-48H | Hemodialysis | CRRT |
|---|---|---|---|---|---|
| **Peak** | 30 minutes after 3rd dose* | 30 minutes after 3rd dose* | 30 minutes after 2nd dose* | 30 minutes after 2nd dose*<br>▪ target peak Cp post HD ~ 8mg/L (6-10 mg/L) | 30 minutes after 2nd dose* |
| **Trough** | 30-60 minutes before 4th dose | 30-60 minutes before 3rd dose | 30-60 minutes before 2nd dose | Immediately *before* HD; Redose for pre-HD:<br>▪ Cp< 1mg/L (mild UTI and synergy)<br>▪ Cp< 2-3mg/L (moderate-severe UTI)<br>▪ Cp< 3-5mg/L (severe GNR infection) | 30-60 minutes before 3rd dose |

**Gram-Positive Synergy**

| | Q8H | Q12H | Q24-48H | Hemodialysis | CRRT |
|---|---|---|---|---|---|
| **Trough** | 30-60 minutes before the 4th dose | 30-60 minutes before the 3rd dose | 30-60 minutes before the 2nd dose | Immediately *before* HD; Redose for pre-HD: Cp<1mg/L | 30-60 minutes before 3rd dose |

*Peaks are drawn 30 minutes after the end of the infusion; Cp = concentration in plasma

**Target Levels based on Dosing Regimen**

| | Gentamicin and Tobramycin | | | | Amikacin | | |
|---|---|---|---|---|---|---|---|
| **Dose** | 1mg/kg | 1.5-2mg/kg | 7mg/kg* | 10 mg/kg** | 5-7.5mg/kg | 15mg/kg | 20 mg/kg** |
| **Usual Interval** | Q8H | Q8H | Q24H*** | Q24H | Q12H | Q24H*** | Q24H*** |
| **Peak** | 3-5 | 4-8 | 20-25 | 20-30 | 20-35 | 35-50 | 40-60 |
| **Trough** | <1 | <1-2 | <1 | <1 | <5-8 | <4 | <4 |

*7mg/kg once daily dosing does not require routine monitoring of target peaks and troughs unless the patient is having fluctuations in renal function or has failed extended interval dosing. Please follow the Hartford nomogram and check an 8-12 hour post-dose level, this can be done after the first dose

**This dose is generally used for cystic fibrosis patients

*** Extended interval dosing can be Q24H, Q36H, or Q48H

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