

## TITLE: AMINOGLYCOSIDE EXTENDED INTERVAL DOSING AND MONITORING IN ADULTS

This is an alternative dosing method which may be less nephrotoxic than conventional dosing with similar efficacy. The higher peak concentrations achieved with this high-dose method may result in a more rapid killing of organisms due to the concentration-dependent killing observed with aminoglycosides. The lower trough concentrations may result in a potentially lower incidence of toxicity.

**Single-daily high dose aminoglycoside therapy should not be confused with patients receiving conventional dosing methods (1 to 2 mg/kg/day) for whom the dosing interval has been adjusted to every 24 hours because of renal dysfunction.**

The following are conservative guidelines for the selection, dosing, and monitoring of extended interval ("once daily") dosing of aminoglycosides adapted from published pharmacokinetic and pharmacodynamic literature.

### Exclusion criteria:

Elderly (age $\geq$ 70 years)	Endocarditis
Pregnancy or post-partum	Synergy for gram positive infections
Renal insufficiency (CrCL < 30 ml/min)	Cystic fibrosis*
Dialysis	Surgical prophylaxis
Severe liver disease or ascites	Severe fluid overload states
History or signs of hearing loss or vestibular toxicity	Extensive burns (> 50% total body surface area)

\* Due to altered volumes of distribution and clearance, patients with cystic fibrosis often require higher doses of aminoglycosides (gentamicin/tobramycin: 7-10 mg/kg/day; amikacin: 25-30 mg/kg/day)

**IMPORTANT: DO NOT USE TOTAL BODY WEIGHT UNLESS PATIENT'S ACTUAL WEIGHT IS LESS THAN THEIR IDEAL WEIGHT**

### 1. Determine patient's dosing weight (DW)

- Non-Obese patients: Use ideal body weight (IBW) unless total body weight (TBW) is less. Non-obese is defined as TBW < 30% over ideal body weight
  - IBW (males) = 50 kg + (2.3 x height in inches > 60 inches)
  - IBW (females) = 45 kg + (2.3 x height in inches > 60 inches)
- Obese patients: Use adjusted body weight (ABW) in obese patients (TBW > 30% over IBW)
  - ABW (kg) = IBW + 0.4 (TBW - IBW)

### 2. Determine patient's dose

(round to nearest 20 mg for gentamicin/tobramycin and to nearest 100 mg for amikacin)

- Gentamicin / Tobramycin 5 to 7 mg/kg x DW
- Amikacin 15 to 20 mg/kg x DW

### 3. Estimate patient's creatinine clearance (CrCL)

- CrCL (male) ml/min =  $\frac{140 - \text{age}}{72} \times \text{DW (kg)}$  ( x 0.85 for females)

(Use minimum SCr of 1 mg/dL. Certain disease states or other factors may alter the relationship between SCr and CrCL resulting in over- or under- estimation of CrCL)

### 4. Determine patient's dosing interval based on CrCL

CrCL (ml/min)	Interval (hrs)
> 50	q24h
30 - 50	q36h
< 30	Not eligible, use conventional dosing

### 5. Serum concentration monitoring

**Use trough levels (peak levels NOT routinely monitored):**

- Trough concentrations should be checked 30 to 60 minutes prior to the next (second) dose. Desired levels:
  - Gentamicin / tobramycin < 0.5 mcg/mL
  - Amikacin < 2.5 mcg/mL
- If level is greater than desired trough, extend dosing interval by 12 hours and repeat level prior to next dose (or use conventional dosing and monitoring methods). If the next level continues to be high, then change to conventional dosing method.
- Repeat level weekly OR with any significant changes in renal function. Serum creatinine should be monitored every 1-3 days