ONCE DAILY AMINOGLYCOSIDE DOSING GUIDELINES

Background
Several clinical studies suggest that once-daily aminoglycoside (ODA) dosing is as efficacious with similar toxicity to conventional multiple-daily administration. The rationale for ODA is based on the concentration-dependent kill characteristic of aminoglycosides. At ~10 times the minimum concentration necessary for inhibition of bacterial growth, maximal antimicrobial activity is observed. After this exposure, inhibition of bacterial growth continues for hours despite aminoglycoside concentrations falling below the minimum inhibitory concentration. These two factors enable aminoglycosides to be dosed once daily for the treatment of gram-negative infections.

Inclusion
Patients ordered ODA for prophylactic, empiric, or documented infective treatment.
(Pharmacy will continue to process aminoglycoside prescriptions that are ordered as conventional multiple-daily dosing).

Exclusion
1. Patients with burns on > 20% of body surface
2. Pregnant patients
3. Patients on dialysis
4. Patients in septic shock.

Recommended Dose
Gentamicin or tobramycin 6 mg/kg IV (range 5 to 7 mg/kg)
Amikacin or streptomycin 15 mg/kg IV
The dose is administered in 50-100 mL NS or D5W IV over 30 minutes.

Dosage should be based on the ideal body weight (IBW). In obese patients (>125% of the IBW), the dosage is based on the IBW plus 40% of estimated adipose tissue mass [IBW + 0.4 (TBW-IBW)].

Dosing interval
Dosing interval is adjusted based on the estimated or measured creatinine clearance.

Creatinine Clearance mL/min	Dosing Interval
≥ 60	Q24h
40-59	Q36h (pre-dose level recommended)
< 40	Recommended to avoid aminoglycosides. If necessary, use conventional aminoglycoside dosing: 2 mg/kg load followed by 2 post-dose levels taken at least 12-24 hours apart to determine dosing interval

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Cystic fibrosis dosing (CrCl ≥ 60 mL/min): 10 mg/kg IV Q24H, maximum of 660 mg/day unless previous use indicates otherwise. Monitor levels to adjust dose, target peak concentration is 20 to 30 mg/L and target trough concentration is less than 1 mg/L.

Monitoring
The correlation between serum aminoglycoside concentrations with once daily dosing and clinical outcomes has not been intensively studied, and pharmacokinetic monitoring itself has not been shown to improve efficacy or prevent toxicity. Some literature have shown high variability in estimated pharmacokinetic parameters of aminoglycosides with once-daily dosing and other studies have reported that in some patients, nomograms often do not accurately predict the correct dose or dosing interval. Therefore, selective pharmacokinetic monitoring may be required.

1. In all patients, twice weekly serum creatinine measurements are recommended to assess renal function.
2. For patients with a creatinine clearance < 60 mL/min, a pre-dose aminoglycoside level may be warranted to ensure that levels are negligible (< 1 mg/L) at the end of the dosing period. Levels can be drawn prior to second or third dose.
3. *Baseline and weekly audiometry and the E-test are recommended for patients who require greater than 2 weeks of aminoglycoside therapy.* (Please call local 54005 for the Otolaryngology and Neuro-otology Unit, Department of Surgery for an appointment).