

Aminoglycosides

Background

Aminoglycosides (AMG) are a class of antimicrobials that can be used for the treatment of:

- ✎ Gram-negative infections (often reserved for multi-drug resistant organisms)
- ✎ Gram-positive infections, when used in combination with cell wall active agents (e.g. beta-lactams, vancomycin) for synergy

There are various dosing strategies available for AMGs:

- ✎ Once daily dosing (extended-interval)
- ✎ Multiple daily dosing (traditional)
 - Synergy dosing

The once daily dosing regimen is recommended for most infections. Based on a lack of published experience, it should not be used in the situations listed below. Instead, the multiple daily dosing strategy should be employed.

- ✎ Renal dysfunction (CrCl < 40 ml/min)
- ✎ Ascites
- ✎ Burns (>20% BSA involvement)
- ✎ Deep-seated infections (e.g. Endocarditis, meningitis, osteomyelitis)
- ✎ Pregnancy
- ✎ Synergistic therapy
- ✎ Septic shock (during initial hemodynamic instability)

Once Daily Dosing (ODD)

Dosing Regimen

- ✎ Dosing is based on actual body weight
 - In obese patients (>30% above ideal body weight), dose based on adjusted body weight
- ✎ Consider high end of dosing range for treatment of severe infections/critically ill patients

Aminoglycoside	Creatinine Clearance (mL/min)		
	≥ 60	40-59	< 40
Gentamicin [†] & Tobramycin _(NF) 5-7 mg/kg (round to nearest 20 mg)	q24h	q36h	Use MDD
Amikacin _(NF) 15 mg/kg (round to nearest 25 mg)			

† Preferred Osler Agent

MDD – Multiple daily dose regimen

NF – Non-formulary agent that requires approval prior to dispensing

Target Trough Levels & Therapeutic Drug Monitoring

Once daily regimens often only require **trough** monitoring as peak targets are likely achieved with larger doses

Trough levels

- ✎ Obtain 30 min prior to administration of the next dose
- ✎ For patients undergoing hemodialysis, trough levels should be obtained prior to dialysis session
- ✎ First trough level should be obtained prior to the 2nd dose

Repeat levels

- ✎ If prolonged therapy is expected (i.e. > 5 days) trough levels should be repeated weekly

Target levels

Aminoglycoside	Peak (mg/L)	Trough (mg/L)
Gentamicin	≥ 20	< 0.5
Tobramycin	≥ 20	< 0.5
Amikacin	≥ 40	< 1

Aminoglycosides

Traditional/Multiple Daily Dosing (MDD)

Dosing Regimen

- Dosing is based on actual body weight
 - In obese patients (>30% above ideal body weight), dose based on adjusted body weight
- Consider high end of dosing range for treatment of severe infections/critically ill patients

	Creatinine Clearance (CrCl) mL/min					
	>60	40-59	20-39	<20	HD	CRRT
Gentamicin[†] & Tobramycin_(NF) 1-2 mg/kg (round to nearest 20 mg)	q8h	q12h	q24h	Based on levels	post HD	q24-48hr
	>40	<40		HD	CRRT	
Amikacin_(NF) - 7.5 mg/kg (round to nearest 25 mg)	q12h	q24h		post HD	q24-48hr	

[†] Preferred Osler Agent

HD – Hemodialysis

CRRT – Continuous renal replacement therapy

NF – Non-formulary agent that requires approval prior to dispensing

Target Trough Levels & Therapeutic Drug Monitoring

The multiple daily dosing regimen requires **both trough** and **peak** levels for proper pharmacokinetic monitoring.

Trough levels

- Obtain 30 min prior to administration of the next dose
- For patients undergoing hemodialysis, trough levels should be obtained prior to dialysis session
- First trough level should be obtained prior to the 3rd dose

Peak level

- Obtain 30 min after the completion of infusion
- Peak level should be obtained after the 3rd dose

Repeat levels

- A set of peak and trough levels should be obtained every 7 days
- Increased monitoring may be required in patients with fluctuating renal function

Target levels

Aminoglycoside	Peak (mg/L)	Trough (mg/L)
Gentamicin	4-10	<2*
Tobramycin	4-10	<2*
Amikacin	15-30	<10

* In severe gram-negative infections, pre-dialysis trough targets can be <3-5mg/L

Dosing for Synergy

Indication

Gentamicin can be used in combination with a cell wall agent (e.g. beta-lactams, vancomycin) in the setting of infective endocarditis due to gram-positive pathogens.

Dosing Regimen

Gentamicin 1mg/kg q8h

*Adjust dosing interval based on renal dysfunction – see above MDD dosing recommendations

Target Trough Levels & Therapeutic Drug Monitoring

Gentamicin target levels

Peak (mg/L)	Trough (mg/L)
3-5	<1

Aminoglycosides

Monitoring & Adverse Events

Routine monitoring is recommended for all patients receiving aminoglycoside therapy.

Renal function

- ✎ The following tests are recommended 3x/week:
 - Serum creatinine
 - BUN
- ✎ Nephrotoxicity (>25% increase from baseline) is associated with elevated trough levels – re-assessing the need for ongoing aminoglycoside therapy is recommended.
- ✎ Combination of aminoglycosides with other nephrotoxic agents (e.g. Vancomycin) can increase the likelihood of adverse events.

Ototoxicity

- ✎ Ongoing aminoglycoside therapy can cause ototoxicity and result in vestibular & cochlear function
- ✎ Ototoxicity has not been shown to be related to peak or trough serum levels
- ✎ Patients should receive regular otology testing to assess for aminoglycoside ototoxicity

Appendix

Ideal Body Weight

IBW (male) = 50.0 kg + 2.3 kg (each inch > 5 feet)

IBW (female) 45.5 kg + 2.3 kg (each inch > 5 feet)

Adjusted Body Weight

Used if actual body weight ≥ 30% above IBW

ABW = IBW + 0.4 (actual body weight – IBW)