Initiating Intravenous (IV) Aminoglycoside Therapy Safely in Adult Inpatients

Version 2.8
Version Date: 28 February 2025

UHN Canada's Hospital

Approved by:
UHN P&T: 5 June 2023
UHN MAC:6 July 2023
Sinai Health P&T: 16 June 2023
Sinai Health MAC: 6 September 2023

Table of Contents

This is a hyperlinked document, start with Background and follow the links to navigate

Background Page 3
What you need to know… Page 4

Direct Section Links

Specific Drug and Syndrome Information
Empiric or targeted treatment of infections due to gram negative bacteria including obstetrics and gynecologic infections Page 5
Tobramycin/Gentamicin
Amikacin
Treatment of infections due to non-tuberculous Mycobacterium spp. Page 12
Amikacin
Synergy for infections due to gram positive bacteria Page 15
Gentamicin
Specific Patient Populations
Critically Ill patients
Tobramycin/Gentamicin Page 6
Amikacin Page 9
Patients with Cystic Fibrosis Page 18
Supporting Information
Neurotology Consultation Page 19
Patient Consent Information Page 20

Background

Aminoglycosides are antimicrobials usually reserved for treatment of gram negative organisms not susceptible to other, less toxic antibiotic therapy. Aminoglycosides may very rarely be used in combination with other antimicrobials ("synergy") in select infections due to gram positive bacteria such as *Enterococcus spp*. infective endocarditis.

Aminoglycosides are associated with potentially serious adverse effects including ototoxicity (cochleo- and vestibulotoxicity), nephrotoxicity and neuromuscular blockade (in patients with myasthenia gravis).

Ototoxicity is exposure dependent, is usually irreversible and occurs in as many as 20-40% of patients on prolonged therapy.

Nephrotoxicity is dose and duration dependent, is usually reversible and occurs in ~15% of patients.

Short course (i.e.<3 days) empiric therapy is unlikely to cause significant ototoxicity or nephrotoxicity In most patients.

Definitions and Abbreviations

Extended Interval Dosing	also referred to as "once daily dosing", this refers to a high-dose, less frequent administration of aminoglycoside to optimize bacterial killing and reduce nephrotoxicity
Traditional Dosing	also referred to as "multiple daily dosing", this refers to smaller, more frequent doses of aminoglycosides (usually twice to thrice daily)
Empiric Therapy	antimicrobials given before the causative organisms is isolated
Targeted Therapy	antimicrobials given after isolation of a causative organism
Peak Level	An aminoglycoside level drawn approximately 30 minutes AFTER the end of an aminoglycoside dose
Trough Level	An aminoglycoside blood level drawn immediately BEFORE the next scheduled aminoglycoside dose
Random Level	An aminoglycoside level drawn without regard to the dosing interval, peak or trough levels
CrCl	Creatinine Clearance (estimated by the Cockcroft-Gault equation)
IHD	Intermittent Hemodialysis
PD	Peritoneal Dialysis
CRRT	Continuous Renal Replacement Therapy
SLED	Sustained Low-Efficiency Dialysis

.

Dosing recommendations in this document refer to the intravenous (IV) route of administration

For patients on **peritoneal dialysis (PD) with peritonitis**, the intraperitoneal (IP) route is preferred.

For the management of PD peritonitis and IP aminoglycoside dosing recommendations, please refer to the UHN Division of Nephrology House Staff/NP guidebook on the Nephrology Home Page and consult Nephrology

What you need to know…

1. **Contraindications**
    a. Allergy to any aminoglycoside or components
    b. Myasthenia gravis
    c. Known genetic predisposition to aminoglycoside ototoxicity (i.e. specific mitochondrial mutations (ex. m. 1555A>G mutation)

2. **Comorbidity** (reasons to avoid extended interval dosing)
    a. Renal impairment or dialysis
    b. Ascites / Cirrhosis
    c. Pregnancy
    d. Large burn area (>20% BSA)
    e. Cystic fibrosis

3. **Anthropometrics**
    a. Total (Actual) Body Weight (TBW)
    b. Height
    c. Ideal Body Weight (IBW, Devine equation)
        i. Males: 50 kg + (2.3 x height per inch > 60 inches)
        ii. Females: 45.5 kg + (2.3 x height per inch > 60 inches)
    d. %IBW: (Actual Body Weight (kg) – Ideal Body Weight (kg))/Ideal Body Weight (kg)

4. **Kidney Function**
    a. Creatinine Clearance (using Cockcroft-Gault equation):
        i. Males: [(140-age) x ideal body weight]/ serum creatinine (mmol/L) x 1.2
        ii. Female: [(140-age) x ideal body weight]/ serum creatinine (mmol/L) x 1.2 x 0.85
        (Note: while other equations have been proposed and may be better reflective of renal function, Cockcroft-Gault continues to be the standard by which aminoglycosides are dosed)
    b. Urine output: if possible, gather information about current and past urine output to estimate stability of renal function

5. **Indication/Antimicrobial**
    a. Empiric or targeted treatment of infections due to gram negative bacteria (including obstetrics and gynecologic infections)
        i. Gentamicin/Tobramycin
        ii. Amikacin
    b. Treatment of infections due to non-tuberculous *Mycobacterium spp.*
        i. Amikacin
    c. Synergy for infections due to gram positive bacteria
        i. Gentamicin

Tobramycin/Gentamicin for treatment of infections due to gram negative bacteria

What you need to do…

1. **Determine dosing weight**

If patient is:	Then use:
Less than ideal body weight	Total (Actual) Body Weight (TBW)
100 to 130% of ideal body weight	Ideal body weight (IBW)
>130% of ideal body weight	Adjusted body weight (AdjBW) AdjBW=IBW + 0.4(TBW – IBW)

2. **Choose a situation/dosing strategy**
   a. Patients without cystic fibrosis
      i. Extended Interval Dosing (choose ***UNLESS*** any of the following)
         (1) Renal impairment (CrCl<20 ml/min)
         (2) Ascites / Cirrhosis
         (3) Pregnancy
         (4) Large burn area (>20% BSA)
      ii. Traditional Dosing (if unable to use Extended Interval Dosing)
   b. Patients with cystic fibrosis

Tobramycin/Gentamicin extended interval dosing for treatment of infections due to gram negative bacteria

***Note: Gentamicin is no longer recommended for the treatment of infections caused by *Pseudomonas aeruginosa*.**

***Note: In critically ill patient's ≤130% IBW, use total body weight dosing to account for increased Vd. For patients >130% IBW, continue to use adjusted body weight.**

Patients with renal dysfunction along with changes to volume of distribution often have significantly altered pharmacokinetic parameters. Frequent monitoring of urine output, serum creatinine and aminoglycosides are suggested.

Initial Dose (regardless of renal function or dialysis timing)

Indication	Dose
Upper urinary tract infection, intra-abdominal infection, febrile neutropenia, pneumonia, septic shock NYD	7 mg/kg

(note: round to nearest 20mg increment)

Maintenance Dose Frequency

- CrCl ≥ 60 ml/min: q24h
- CrCl 40-59 ml/min: q36h
- CrCl 20-39 ml/min, SLED, IHD or CRRT: q48h (ideally administered pre-dialysis) (NOTE: clearance between different patients and dialysis modalities is highly variable, dose adjustment by level and type/frequency of dialysis is essential)
- CrCl <20 ml/min: use traditional dosing strategy and dose by level

Monitoring

Most patients using empiric therapy for the coverage of gram negative infections do not require therapeutic drug monitoring (TDM) as therapy will be discontinued within 72 hours. If therapy is to continue longer than 72 hours, TDM should be done, informed consent obtained and neurotology consultation obtained.

Trough only monitoring is acceptable for extended interval dosing. If dose reduction is required, peak monitoring should be done (refer to traditional dosing).

1. **Serum creatinine** at baseline and three times weekly while on therapy

2. **Therapeutic Drug Monitoring (TDM)**

Renal Function/Dialysis	**Trough level timing**	**Re-dose if trough…**
CrCL > 60 ml/min	30 min prior to 3rd dose	<1 mg/L (ideally undetectable)
CrCl ≤ 60 ml/min	30 min prior to 2nd dose	<1 mg/L (ideally undetectable)
Intermittent SLED/IHD	30 min prior to next scheduled dialysis session	< 2 mg/L (ideally undetectable)
CRRT or continuous SLED	24 hours after 1st dose	< 1 mg/L (ideally undetectable)

Trough Level Timing:
<30 minutes before next dose

Tobramycin/Gentamicin traditional dosing for infections due to gram negative bacteria

***Note: Gentamicin is no longer recommended for the treatment of infections caused by *Pseudomonas aeruginosa*.**

Dose (note: round to nearest 20mg increment)

CrCl ≥ 20ml/min	1.7 mg/kg
IHD	2mg/kg load, then 1mg/kg post IHD
PD	1.7 mg/kg (if using for PD peritonitis, see nephrology PD guideline)
CRRT	Suggest extended interval dosing
SLED	1.7 mg/kg For durations of SLED longer than 8-12h, suggest extended interval dosing.

Frequency

- CrCl > 60 ml/min: q8h
- CrCl 40-60 ml/min: q12h
- CrCl 20-39 ml/min: q24h
- CrCl <20 ml/min: dose by level

Dialysis

- IHD: post-IHD (after initial load)
- PD: dose by level
- CRRT: Suggest extended interval dosing
- SLED: generally, q24h (see dosing)

Monitoring

Most patients using empiric therapy for the coverage of gram-negative infections do not require therapeutic drug monitoring (TDM) as therapy will be discontinued within 72 hours. If therapy is to continue longer than 72 hours, TDM should be done, informed consent obtained and neurotology consultation obtained.

1. **Serum creatinine** at baseline and three times weekly while on therapy
2. **TDM**
   - CrCl >60 ml/min: peak post-3rd dose, trough pre-4th dose
   - CrCl 20 – 59 ml/min: peak post 2nd dose, trough pre-3rd dose
   - CrCl <20 ml/min: peak post 2nd dose, trough before each dose

   Dialysis
   - IHD: trough pre-IHD before next IHD session
   - PD: peak post 2nd dose, trough before each dose
   - CRRT: peak after 2nd dose, trough pre-3rd dose
   - SLED: peak after 2nd dose, trough pre-3rd dose

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

Target (non-IHD)

- Severe infection (ex. pneumonia): peak 8-10 mg/L, trough 1-2 mg/L
- Other infections: peak 6-8 mg/L, trough 1-2 mg/L
- Cystitis: peak 4-6 mg/L, trough 1-2 mg/L

Target (patients on IHD)

- Pre-dialysis levels should generally be between 1-2 mg/L, but may be higher in more severe infections, consult a clinical pharmacist for information
- Post-dialysis levels are not typically done

Amikacin for infections due to gram negative bacteria

What you need to do…

1. **Determine dosing weight**

If patient is:	Then use:
Less than ideal body weight	Total (Actual) Body Weight (TBW)
100 to 130% of ideal body weight	Ideal body weight (IBW)
>130% of ideal body weight	Adjusted body weight (AdjBW) AdjBW=IBW + 0.4(TBW – IBW)

2. **Choose a situation/dosing strategy**
   a. Critically ill patients (including those with cystic fibrosis)
   b. Non-critically ill patients with cystic fibrosis
   c. Other non-critically ill patients
      i. Extended Interval Dosing (choose ***UNLESS*** any of the following)
         (1) Renal impairment (CrCL<20 ml/min) or dialysis
         (2) Ascites / Cirrhosis
         (3) Pregnancy
         (4) Large burn area (>20% BSA)
      ii. Traditional Dosing (if unable to use Extended Interval Dosing)

Amikacin in <u>critically ill patients</u> for treatment of infections due to gram negative bacteria

***Note: amikacin is no longer recommended for infections caused by *Pseudomonas aeruginosa* outside of the urinary tract.**

In critically ill patient's ≤130% IBW, use total body weight dosing to account for increased Vd. For patients >130% IBW, continue to use adjusted body weight.

Patients with renal dysfunction along with changes to volume of distribution often have significantly altered pharmacokinetic parameters. Frequent monitoring of urine output, serum creatinine and aminoglycosides are suggested.

Note that not all patients in the ICU will require this approach. In patients who are stable and not in a profound vasodilatory state, consider using a more routine dosing approach as outlined elsewhere in this document.

Initial Dose (regardless of renal function or dialysis timing)

Indication	Dose
Upper urinary tract infection, intra-abdominal infection, febrile neutropenia	15 mg/kg
Pneumonia, Septic Shock	25 mg/kg
Patients with cystic fibrosis	35 mg/kg

(Note: round to the nearest 20mg increment)

Frequency

- CrCl > 60 ml/min: q24h
- CrCl 40-59 ml/min: q36h
- CrCl 20-39 ml/min, SLED, IHD and CRRT: q48h (adjust dose by level) (NOTE: clearance between different patients and dialysis modalities is highly variable, dose adjustment by level and type/frequency of dialysis is essential)
- CrCl <20 ml/min: adjust dose by level

Monitoring

Most patients using empiric therapy for the coverage of gram-negative infections do not require therapeutic drug monitoring (TDM) as therapy will be discontinued within 72 hours. If therapy is to continue longer than 72 hours, TDM should be done, informed consent obtained and neurotology consultation obtained.

Trough Level Timing: <30 minutes BEFORE next dose

Trough only monitoring is acceptable for extended interval dosing. If dose reduction is required, peak monitoring should be done (refer to traditional dosing).

1. **Serum creatinine** at baseline and three times weekly while on therapy
2. **TDM**

Renal Function/Dialysis	Trough level timing	Re-dose if trough…
CrCL > 60 ml/min	Prior to 3rd dose	<2.3 mg/L
CrCl ≤ 60 ml/min	Prior to 2nd dose	<2.3 mg/L
intermittent SLED/IHD	Prior to next scheduled dialysis session	< 4-8 mg/L
CRRT or continuous SLED	24 hours after 1st dose	< 2.3 mg/L

Amikacin extended interval dosing for infections due to gram negative bacteria

***Note: amikacin is no longer recommended for infections caused by *Pseudomonas aeruginosa* outside of the urinary tract.**

Dose (Note: round dose to nearest 50 mg increment)
- 15 mg/kg

Frequency
- CrCl ≥ 60 ml/min: q24h
- CrCl 40 - 59 ml/min: q36h
- CrCl 20 – 39 ml/min: q48h
- CrCl <20 ml/min use traditional dosing strategy

Monitoring

Most patients using empiric therapy for the coverage of gram-negative infections do not require therapeutic drug monitoring (TDM) as therapy will be discontinued within 72 hours. If therapy is to continue longer than 72 hours, TDM should be done, informed consent obtained and neurotology consultation obtained.

Trough Level Timing: <30 minutes BEFORE next dose

1. **Serum Creatinine** at baseline and three times weekly while on aminoglycoside therapy
2. **TDM**
   - CrCl > 60 ml min: pre-dose level 30 minutes before the 3rd dose
   - CrCl < 60 ml min: pre-dose level 30 minutes before 2nd dose

Target
- Trough < 2.3 mg/L (undetectable)

Amikacin traditional dosing for infections due to gram negative bacteria

***Note: amikacin is no longer recommended for infections caused by *Pseudomonas aeruginosa* outside of the urinary tract.**

Dose (Note: round dose to nearest 50mg increment)

CrCl ≥ 20ml/min	5 - 7.5 mg/kg
CrCl < 20 ml/min	5 mg/kg load, then dose by level
IHD	5 – 7.5 mg/kg post-IHD
PD	5 - 7.5 mg/kg (if using for PD peritonitis, see nephrology PD guideline)
CRRT	Suggest extended interval dosing
SLED	7.5 mg/kg For durations of SLED longer than 8-12h, consider extended interval dosing.

Frequency

- CrCl > 60 ml/min: q8h
- CrCl 40 - 59 ml/min: q12h
- CrCl 20-39 ml/min: q24h
- CrCl <20 ml/min: dose by level

Dialysis

- IHD: post-IHD (after initial load, dose by level)
- PD: dose by level
- CRRT: suggest extended interval dosing
- SLED: generally, q24h (see dosing)

Monitoring

Most patients using empiric therapy for the coverage of multi-drug resistant gram-negative infections do not require therapeutic drug monitoring (TDM) as therapy will be discontinued within 72 hours. If therapy is to continue longer than 72 hours, TDM should be done, informed consent obtained and neurotology consultation obtained.

1. **Serum creatinine** at baseline and three times weekly while on therapy
2. **TDM**
   - CrCl > 60 ml/min: peak post-3rd dose, trough pre-4th dose
   - CrCl 20 – 59 ml/min: peak post 2nd dose, trough pre-3rd dose
   - CrCl <20 ml/min: level should generally be drawn before each dose

Dialysis

- IHD: trough pre-IHD before next IHD session
- PD: peak after 2nd dose, trough before each dose
- CRRT: peak after 2nd dose, trough pre-3rd dose
- SLED: peak after 2nd dose, trough pre-3rd dose

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

Target (non-IHD)

- Pneumonia: Peak 20-30 mg/L Trough 4-8 mg/L
- Other infections: Peak 20-25 mg/L, Trough 4-8 mg/L
- Cystitis: Peak 15-20 mg/L, Trough 4-8 mg/L

Target (IHD)

- Pre-dialysis levels should be tailored to the severity of infection and should generally be between 4-8 mg/L
- Post-dialysis levels are not typically done

Amikacin for treatment of non-tuberculous *Mycobacterium spp.*

What you need to do...

1. **Determine dosing weight**

If patient is:	Then use:
Less than ideal body weight	Total (Actual) Body Weight (TBW)
100 to 130% of ideal body weight	Ideal body weight (IBW)
>130% of ideal body weight	Adjusted body weight (AdjBW) AdjBW=IBW + 0.4(TBW – IBW)

2. **Choose a dosing strategy**
    a. Traditional (daily) dosing
    b. Three times weekly dosing

Amikacin traditional (daily) dosing for treatment of non-*tuberculous Mycobacterium spp.*

(Note: management of mycobacterial disease is complex, required combination therapy with multiple antimicrobials and skill/experience in the area. Expert consultation strongly advised.)

Dose (Note: round dose to nearest 50mg increment)

- 8-15 mg/kg

Frequency

- CrCl > 60 ml/min: q24h
- CrCl 40 - 59 ml/min: q24-48h
- CrCL 30 - 39 ml/min/CRRT/SLED: q48-72h
- CrCl <30 ml/min/IHD: dose by level

Monitoring

As patients will be receiving protracted therapy, therapeutic drug monitoring (TDM) is warranted in all patients. Informed consent should be obtained and neurotology consultation obtained.

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

1. **Serum Creatinine**: baseline, then three times weekly while in hospital
2. **TDM**
   - Peak after 1st dose
   - Trough before 2nd dose
   - Repeat trough weekly or with renal function c hanges while in hospital

Target

- Peak: 20-35 mg/L
- Trough: < 2.3 mg/L (undetectable)

Amikacin three times weekly dosing for treatment of non-*tuberculous Mycobacterium spp.*

(Note: management of mycobacterial disease is complex, required combination therapy with multiple antimicrobials and skill/experience in the area. Expert consultation strongly advised.)

Dose (Note: round dose to nearest 50mg increment)

- 8-15 mg/kg

Frequency

- CrCl ≥ 30 ml/min: three times weekly
- CrCl < 30 ml/min, any dialysis modality: dose by level

Monitoring

As patients will be receiving protracted therapy, therapeutic drug monitoring (TDM) is warranted, Informed consent should be obtained and neurotology consultation obtained.

1. **Serum Creatinine:** baseline, then three times weekly while in hospital
2. **TDM**
   - Peak after 1st dose
   - Trough before 2nd dose
   - Repeat trough weekly or with renal function changes while in hospital

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

Target

- Peak: 20-35 mg/L (may consider higher levels in select patients)
- Trough: < 2.3 mg/L (undetectable)

Gentamicin synergy for gram positive bacteria

What you need to do…

1. Determine dosing weight

If patient is:	Then use:
Less than ideal body weight	Total (Actual) Body Weight (TBW)
100 to 130% of ideal body weight	Ideal body weight (IBW)
>130% of ideal body weight	Adjusted body weight (AdjBW) AdjBW=IBW + 0.4(TBW – IBW)

2. Confirm indication for therapy

a. Streptococcus spp. infective endocarditis
b. Enterococcus/Staphylococcus spp. infective endocarditis

Gentamicin synergy for *Streptococcus spp.* infective endocarditis

Dose and Frequency (Note: round dose to nearest 20mg increment)

CrCl	Dose and Frequency
>60 ml/min	3 mg/kg q24h
40 – 59 ml/min	1 mg/kg q12h
20 – 39 ml/min	1 mg/kg q24h
<20 ml/min	1 mg/kg (dose by level)
Dialysis	
IHD	1 mg/kg post-IHD (dialysis days only)
PD	1 mg/kg q48h (dose by level)
CRRT	1 mg/kg q24h
SLED	1 mg/kg q12-24h (SLED duration dependent)

Monitoring: As patients will be receiving protracted therapy, therapeutic drug monitoring (TDM) is warranted in all patients. Informed consent should be obtained and neurotology consultation obtained.

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

1. **Serum Creatinine:** baseline, then three times weekly while in hospital
2. **TDM**
   - CrCl ≥ 60 ml/min: trough ONLY, before 3rd dose
   - CrCl 20 – 59 ml/min/SLED/CRRT: peak post 2nd dose, trough pre-3rd dose
   - CrCl <20 ml/min/PD/IHD: Peak post 2nd dose. Trough levels should generally be drawn 24 hours after first dose. Re-dose when level less than 1 mg/L.

Target

- Peak: 3-4 mg/L (not for use with 3mg/kg q24h dosing)
- Trough: < 1 (undetectable preferred if using 3 mg/kg q24h)

Gentamicin synergy for *Staphylococcus/Enterococcus spp.* infective endocarditis

Dose and Frequency (Note: round dose to nearest 20mg increment)

CrCl	Dose and Frequency
>60 ml/min	1 mg/kg q8h
40 – 59 ml/min	1 mg/kg q12h
20 – 39 ml/min	1 mg/kg q24h
<20 ml/min	1 mg/kg (dose by level)
Dialysis	
IHD	1 mg/kg post-IHD (dialysis days only)
PD	1 mg/kg q48h (dose by level)
CRRT	1 mg/kg q24h
SLED	1 mg/kg q12-24h

Monitoring: As patients will be receiving protracted therapy, therapeutic drug monitoring (TDM) is warranted in all patients. Informed consent should be obtained and neurotology consultation obtained.

1. **Serum Creatinine:** baseline, then three times weekly while in hospital
2. **TDM**

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

- CrCl ≥ 60 ml/min: peak after 3rd dose, trough before 4th dose
- CrCl 20 – 59 ml/min/CRRT/SLED: peak post 2nd dose, trough pre-3rd dose
- CrCl <20 ml/min/PD/IHD: Peak post 2nd dose. Trough levels should generally be drawn 24 hours after first dose. Re-dose when level less than 1 mg/L

Target

- Peak: 3 – 4 mg/L
- Trough: < 1 mg/L

Aminoglycoside Dosing in Patients with Cystic Fibrosis

Management of pulmonary infection in patients with cystic fibrosis is complicated by altered aminoglycoside pharmacokinetics and by antimicrobial resistance. As patients with cystic fibrosis have likely been exposed to a number of antimicrobials, including aminoglycosides, careful assessment of antimicrobial resistance and consultation with clinicians experienced in the management of infections in cystic fibrosis is strongly suggested.

Historically, aminoglycosides have been dosed with a traditional dosing method to overcome the increased clearance present in patients with cystic fibrosis. More recent literature has suggested an extended daily dosing/"once daily" dosing approach may be effective and more convenient.

If unable to use extended interval dosing, consult infectious diseases and/or clinical pharmacists.

Of note, inhaled aminoglycoside therapy is not covered in this document.

Dose

- Tobramycin/Gentamicin: 10 mg/kg
  (Note: round to nearest 20mg increment)
- Amikacin: 30-35 mg/kg
  (Note: round to nearest 50mg increment)

Frequency

- CrCl > 60 ml/min: q24h
- CrCl 40-59 ml/min: q36h
- CrCl 20-39 ml/min, SLED and CRRT: q48h (adjust dose by level)
- CrCl <20 ml/min: adjust dose by level
- IHD/PD: consult infectious disease/clinical pharmacist

Monitoring

If therapy is to continue longer than 72 hours, therapeutic drug monitoring (TDM) should be done, informed consent obtained and neurotology consultation obtained.

Peak Level Timing: 30 minutes AFTER then end of the infusion

Trough Level Timing: <30 minutes BEFORE next dose

Lastly, as drug clearance may be higher than anticipated given a degree of renal dysfunction, peak levels should be considered with full pharmacokinetic assessment performed.

1. **Serum creatinine** at baseline and three times weekly while on therapy
2. **TDM**
   - CrCl ≥ 60 ml/min: pre-dose level 30 minutes before the 3rd dose
   - CrCl < 60 ml min: pre-dose level 30 minutes before 2nd dose

Target

- Amikacin: <2.3 mg/L (undetectable)
- Tobramycin/Gentamicin: <1 (preferably undetectable)

Instructions: **For patient at UHN**, please enter a consult into EPIC **AND** fax the following form.
For patients at Mount Sinai, please fax the following form.

UHN Canada's Hospital

Aminoglycosides Assessment Proforma

TGH Multi-Disciplinary Neurotology Clinic

(*Addressograph or fill out patient details*)

Last Name _____

First Name: _____

PMH / TWH / TGH (please circle)

For patients in the community:

Address: _____ Nurse Name: _____

Reason for treatment:

Condition requiring Aminoglycoside treatment: _____ **Medication start date:** _____ / _____ / _____
DD MM YY

Dosing details:

_____ _____ mg _____ times a day, for _____ days
Name of Aminoglycoside Used for Treatment

Comments on Dosing:

Necessary Criteria for Baseline Assessment:
(Please select)

	Y	N
1. Fully conscious and interactive	☐	☐
2. Able to provide consent	☐	☐
3. No major visual impairment	☐	☐

Suitability for specific tests:

Head Shaking Short Rapid Head Oscillations <20◦ (in bed or at bedside)	☐	☐
Posturography Able to stand by bedside unaided	☐	☐

Additional Instructions/comments:

- Hearing and Balance Centre

Pt to have both assessments done as Baseline:

1. Audiogram
2. v-HIT

Signature _____ **Name:** _____

Date: _____ /_____ /_____

Hearing and Balance Centre (416) 340-3666 **Fax referral to (416) 340-3745**

Staff ☐ **Fellow** ☐ **Resident** ☐ **Nurse** ☐ **Pager** _____ **Ext.** _____

This document is for guidance purposes only and does not replace clinical knowledge and judgement when using aminoglycoside therapy. Consultation with clinicians experienced in dosing of aminoglycosides is suggested

Aminoglycoside Safety Information for Discussion with Patients and Caregivers

Disclaimer: this information sheet is meant to serve as a reference to guide an informed consent discussion. It is not a standalone informed consent document

- Aminoglycoside are a group of antimicrobials that include gentamicin, tobramycin and amikacin
- Aminoglycosides are antimicrobial agents used to help treat infections that are often resistant to other antimicrobial agents
- Although used for many years, aminoglycosides may have serious adverse effects
- Aminoglycosides can cause damage to the kidneys (nephrotoxicity) and to the hearing and balance systems of the body (ototoxicity, cochleotoxicity or vestibulotoxicity)
- Ototoxicity can occur in up to 20-40% of patients receiving long-term aminoglycoside therapy and may be irreversible. The risk increases with duration of use.
- Nephrotoxicity occurs in 5-15% of patients receiving aminoglycosides and is usually reversible after stopping drug therapy.
- To help reduce the risk of some of these side effects, your clinical team will monitor your renal function and drug levels of aminoglycosides
- In addition, if you need longer therapy with aminoglycosides, you may need to receive assessment from special hearing and balance clinicians
- While on aminoglycoside therapy, report any hearing changes, balance changes or changes to your gait (the way you walk) immediately

References

1. Bhatt J, Jahnke N, Smyth AR. Once-daily versus multiple-daily dosing with intravenous aminoglycosides for cystic fibrosis. Cochrane Database of Systematic Reviews 2019(9) doi: 10.1002/14651858.CD002009.pub7

2. Boyer A, Timsit JF, Klouche K, et al. Aminoglycosides in Critically Ill Septic Patients With Acute Kidney Injury Receiving Continuous Renal Replacement Therapy: A Multicenter, Observational Study. Clinical therapeutics 2021;43(6):1116-24. doi: 10.1016/j.clinthera.2021.04.011 [published Online First: 2021/05/28]

3. Deelen JWT, Rottier WC, Buiting AGM, et al. Short-course aminoglycosides as adjunctive empirical therapy in patients with Gram-negative bloodstream infection, a cohort study. Clinical Microbiology and Infection 2021;27(2):269-75. doi: https://doi.org/10.1016/j.cmi.2020.04.041

4. Goodlet KJ, Benhalima FZ, Nailor MD. A Systematic Review of Single-Dose Aminoglycoside Therapy for Urinary Tract Infection: Is It Time To Resurrect an Old Strategy? Antimicrob Agents Chemother 2019;63(1) doi: 10.1128/aac.02165-18 [published Online First: 2018/11/07]

5. Halouzková BA, Hartinger JM, Krátký V, et al. Dosing of Aminoglycosides in Chronic Kidney Disease and End-Stage Renal Disease Patients Treated with Intermittent Hemodialysis. Kidney and Blood Pressure Research 2022;47(7):448-58. doi: 10.1159/000523892

6. Illamola SM, Huynh HQ, Liu X, et al. Population Pharmacokinetics of Amikacin in Adult Patients with Cystic Fibrosis. Antimicrob Agents Chemother 2018;62(10) doi: 10.1128/aac.00877-18 [published Online First: 2018/08/01]

7. Logre E, Enser M, Tanaka S, et al. Amikacin pharmacokinetic/pharmacodynamic in intensive care unit: a prospective database. Annals of intensive care 2020;10(1):75. doi: 10.1186/s13613-020-00685-5 [published Online First: 2020/06/10]

8. Marsot A, Hraiech S, Cassir N, et al. Aminoglycosides in critically ill patients: which dosing regimens for which pathogens? International journal of antimicrobial agents 2020;56(4):106124. doi: https://doi.org/10.1016/j.ijantimicag.2020.106124

9. O'Sullivan ME, Perez A, Lin R, et al. Towards the Prevention of Aminoglycoside-Related Hearing Loss. Frontiers in cellular neuroscience 2017;11:325. doi: 10.3389/fncel.2017.00325 [published Online First: 2017/11/03]

10. Ratjen F, Brockhaus F, Angyalosi G. Aminoglycoside therapy against Pseudomonas aeruginosa in cystic fibrosis: a review. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society 2009;8(6):361-9. doi: 10.1016/j.jcf.2009.08.004 [published Online First: 2009/09/15]

11. Roger C, Louart B, Elotmani L, et al. An international survey on aminoglycoside practices in critically ill patients: the AMINO III study. Annals of intensive care 2021;11(1):49. doi: 10.1186/s13613-021-00834-4

12. Sethi SK, Krishnappa V, Nangethu N, et al. Antibiotic Dosing in Sustained Low-Efficiency Dialysis in Critically Ill Patients. Canadian journal of kidney health and disease 2018;5:2054358118792229. doi: 10.1177/2054358118792229 [published Online First: 2018/08/18]

13. Shalit I, Low M, Levy E, et al. Antibiotic use in 26 departments of internal medicine in 6 general hospitals in Israel: variability and contributing factors. J Antimicrob Chemother 2008;62(1):196-204. doi: 10.1093/jac/dkn150 [published Online First: 2008/04/11]

14. Sanford Health Care Aminoglycoside Dosing Guideline [Available from: https://med.stanford.edu/content/dam/sm/bugsanddrugs/documents/antimicrobial-dosing-protocols/SHC-Aminoglycoside-Dosing-Guide.pdf accessed 15 December 2022.

15. South Australia Aminoglycoside Recommendations for Use, Dosing and Monitoring (v3) [Available from:https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/resources/policies/aminoglycosides+recommendations+for+use+dosing+and+monitoring+clinical+guideline accessed December 15 2022.

16. Lexi-Drugs/Amikacin Lexicomp app. Accessed January 30, 2022.

17. Lexi-Drugs/Tobramycin Lexicomp app. Accessed January 30, 2022.

18. Brown P, Battistella M. Principles of Drug Dosing in Sustained Low Efficiency Dialysis (SLED) and Review of Antimicrobial Dosing Literature. Pharmacy (Basel, Switzerland) 2020;8(1) doi: 10.3390/pharmacy8010033 [published Online First: 2020/03/19]

19. Eschenauer GA, Lam SW, Mueller BA. Dose Timing of Aminoglycosides in Hemodialysis Patients: A Pharmacology View. Seminars in dialysis. 2016;29(3):204-13.

20. Jiang M, Karasawa T, Steyger PS. Aminoglycoside-Induced Cochleotoxicity: A Review. Frontiers in cellular neuroscience. 2017;11:308.

21. Dillard LK, Martinez RX, Perez LL, Fullerton AM, Chadha S, McMahon CM. Prevalence of aminoglycoside-induced hearing loss in drug-resistant tuberculosis patients: A systematic review. Journal of Infection. 2021;83(1):27-36.

22. Cobussen M, Haeseker MB, Stoffers J, Wanrooij VHM, Savelkoul PHM, Stassen PM. Renal safety of a single dose of gentamicin in patients with sepsis in the emergency department. Clin Microbiol Infect. 2020.