

## Paediatric Medication Guideline

# Intravenous Aminoglycoside therapy (Amikacin, Gentamicin and Tobramycin)

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Responsible Area	Pharmacy department Infection Management and Prevention Service			Review date	27/02/2025
Executive sponsor	Executive Director Medical Services				
Accountable Officer	Executive Director Clinical Services				

## Purpose

To provide guidance around the clinical use of intravenous amikacin, gentamicin and tobramycin in paediatric patients under the care of/as recommended by Children's Health Queensland (CHQ).

## Scope

This guideline is intended to assist all clinical staff to prescribe, administer and monitor intravenous amikacin, gentamicin and tobramycin appropriately. It is not intended to be a substitute for specific professional or clinical advice, or to replace consultation with senior staff, which should always be sought if clinically relevant.

This material is published by Queensland Health with the intention of providing a guideline for use in paediatric patients under the care of/as recommended by Children's Health Queensland (CHQ). Anyone wishing to use this guideline outside CHQ should refer to their local Medicines Committee before using.

## Description and Indications for Use

Aminoglycosides (amikacin, gentamicin and tobramycin) are highly effective bactericidal antibiotics for parenteral treatment of Gram-negative infections. Due to the potential for nephrotoxicity and ototoxicity, which are more common with increasing duration of use, use should generally be limited to less than 3 doses (72 hour duration), e.g., for empirical treatment of urosepsis.

When given in combination with some cell-wall-active drugs (e.g., penicillins, glycopeptides), aminoglycosides provide useful synergistic killing resulting in higher rate of clinical cure for serious infections such as streptococcal or enterococcal endocarditis.

All patients requiring more than 72 hours of Gentamicin, need Infectious Diseases (ID) input and AMS [approval](#) to receive ongoing therapy. Pre-approved indications for gentamicin and tobramycin are specified on the [CHQ Antimicrobial stewardship website](#). Amikacin is a restricted antimicrobial and requires ID input and AMS [approval](#) prior to prescribing or use.

To ensure efficacy, minimize toxicity and limit the spread of resistance, it is essential that amikacin, gentamicin and tobramycin treatment is prescribed and monitored carefully.



## Prescribing Instructions

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### Contraindications

- Known severe hypersensitivity to aminoglycosides or any of the excipients, but these reactions are rare. If a new reaction occurs, [report and document adverse reaction](#)
- History of aminoglycoside-induced vestibular or auditory toxicity
- Myasthenia gravis (due to risk of neuromuscular blockade)

!

### Precautions

#### Ototoxicity

- Intravenous aminoglycosides should generally not be used in patients with pre-existing significant auditory impairment, a pre-existing vestibular condition or a first-degree relative with aminoglycoside-induced auditory toxicity, since some people have a rare inherited genetic predisposition.
- Risk of ototoxicity is increased with concomitant use of other [ototoxic medications](#).
- For patients with significant risk factors or receiving prolonged courses of aminoglycosides, consider baseline and follow up [audiology screening](#).

#### Nephrotoxicity

- Risk of nephrotoxicity is increased with concomitant use of other nephrotoxic medications and certain comorbidities.

#### Risk factors for toxicity\*:

- Prolonged or repeated aminoglycoside courses
- Dehydration or significant blood loss
- Concomitant nephrotoxic medicines (including glycopeptides, amphotericin, diuretics, ACE inhibitors, NSAIDs, recent IV contrast media, tacrolimus, cyclosporin, nephrotoxic chemotherapy) or [ototoxic medications](#) (including cisplatin, frusemide, aminoglycosides)
- Pre-existing hearing impairment or strong pharmacogenetic predisposition
- Poor renal perfusion due to depressed cardiac function/heart failure/ critical illness/septic shock
- Receiving renal replacement therapy (CRRT, ECMO, Haemodialysis, peritoneal dialysis, plasmapheresis)
- Severe liver disease increasing risk for hepatorenal syndrome
- Renal function and hydration should be closely monitored.
- Pre-existing renal disease, renal impairment and obesity are also risk factors for nephrotoxicity

## Before starting intravenous aminoglycosides

- Check baseline creatinine, urea and electrolytes (CHEM20, CHEM8)
- Assess risk factors for ototoxicity and determine audiology screening requirements
- Assess [renal risk factors](#)\* and renal perfusion (urine output)
- Use Modified Schwartz formula to calculate Paediatric Creatinine Clearance (CrCl)\*\*:

$$\text{CrCl (mL/min/1.73m}^2\text{)} = [36.5 \times \text{Height (cm)}] / \text{Creatinine (micromol/L)} = \text{_____ mL/min/1.73m}^2$$

\*\*Not validated to be used in children under 1 year of age

- Obesity:
  - In patients with a BMI > 95<sup>th</sup> centile for age, use adjusted body weight for dose calculation

$$\text{Adjusted body weight (kg)} = \text{Ideal body weight} + 0.4 \times (\text{Measured Weight} - \text{Ideal body weight})$$

- A child's ideal body weight (IBW) can be estimated using the corresponding weight for the height percentile on the growth chart ( [www.cdc.gov/growthcharts](http://www.cdc.gov/growthcharts) ) or, if the child's height cannot be determined, the average weight-for-age (50th centile) on the growth chart.

## Daily review whilst on intravenous aminoglycoside therapy

Clinicians must answer the following questions DAILY for any patient receiving IV aminoglycosides:

- Is the aminoglycoside the most appropriate IV antibiotic based on clinical condition and microbiology results?
  - If not, is an alternative antibiotic more appropriate? Seek ID advice.
- Is the current dose of aminoglycoside appropriate for indication, renal function and hydration status?
  - If not, perform therapeutic drug monitoring (TDM) and seek expert advice.
  - Is the patient experiencing any signs of vestibular or auditory toxicity for example?
    - gait ataxia and imbalance
    - oscillopsia (the subjective sensation of bouncing vision) or blurred vision during head movement
    - hearing loss.

If vestibular or auditory toxicity is detected, stop the aminoglycoside and seek expert advice.

## Prescribing initial intravenous aminoglycoside dose

**Table 1: Dosing Guidance for initiating intravenous GENTAMICIN**

<b>Before starting:</b>	
<ul style="list-style-type: none"> <li>Perform baseline CHEM20 (Urea, Creatinine, Liver function tests, electrolytes)</li> <li>Obesity: Patients with a BMI &gt;95<sup>th</sup> centile for age – Calculate Gentamicin dose based on Adjusted Body weight</li> <li>Assess renal function and risk factors</li> <li>Assess risk factors for ototoxicity and determine audiology screening requirements</li> </ul>	
Patient population	Initial dose
Neonates	Refer to <a href="#">Australasian Neonatal Medicines formulary (ANMF) – Gentamicin neonatal monograph</a> for dosing information. Note: Neonate on ECMO – Consider alternative antibiotic in consultation with ID. If gentamicin is essential, seek ID/ PICU expert advice on dosing and monitoring.
Infants and children with normal renal function (CrCl >60 mL/min/1.73m <sup>2</sup> )	<b>General infection:</b> <b>More than 1 month to 10 years of age:</b> 7.5 mg/kg IV 24-hourly (Max 320 mg/day initial dose).  <b>More than 10 years to 18 years of age:</b> 6 mg/kg IV 24-hourly (Max 560 mg/day initial dose).  Adjust according to TDM.
	<b>Critically ill/ septic shock:</b> <b>More than 1 month to 10 years of age:</b> 7.5 mg/kg IV 24-hourly (Max 320 mg/day initial dose).  <b>More than 10 years to 18 years of age:</b> 7 mg/kg IV 24-hourly (Max 640 mg/day initial dose).  Adjust according to TDM.
Infants and children with renal insufficiency (CrCl < 60 mL/min/1.73m <sup>2</sup> )	<b>Initial dose:</b> <b>&gt;1 month to 18 years of age:</b> <ul style="list-style-type: none"> <li>General infection: 5 mg/kg IV (Max 320mg)</li> <li>Critically ill/ septic shock: 7 mg/kg IV (Max 560 mg)</li> </ul>
	<b>Creatinine clearance (CrCl) (Modified Schwartz)</b>
	<b>40 to 59 mL/min/1.73m<sup>2</sup></b>
	<b>20 to 39 mL/min/1.73m<sup>2</sup> (including Haemodialysis, CRRT and ECMO)</b>
<b>Less than 20 mL/min/1.73m<sup>2</sup></b>	
	<b>Initial dosing interval</b>  36-hourly dosing Perform TDM. Withhold dose until trough level <1mg/L.  Consider other agents. If essential, give a single IV dose, perform TDM. Withhold dose until trough level <1mg/L. Seek ID/renal/pharmacist advice on re-dosing.  Avoid. Seek ID specialist advice.
Streptococcal or enterococcal infective endocarditis	Synergy with beta-lactam antibiotic. Seek ID advice. >1 month to 18 years of age: 1 to 2 mg/kg/dose IV 8 hourly.
Surgical antibiotic prophylaxis	Refer to <a href="#">CHQ-GDL-01064 CHQ Paediatric surgical antibiotic prophylaxis guidelines</a>

**Table 2: Dosing Guidance for initiating intravenous TOBRAMYCIN**

Table 2: Dosing Guidance for initiating intravenous TOBRAMYCIN		
<b>Before starting:</b>		
<ul style="list-style-type: none"> <li>• Perform baseline CHEM20 (Urea, Creatinine, Liver function tests, electrolytes)</li> <li>• Obesity: Patients with a BMI &gt;95<sup>th</sup> centile for age – Calculate Tobramycin dose based on Adjusted Body weight</li> <li>• Assess renal function and risk factors</li> <li>• Assess risk factors for ototoxicity and determine audiology screening requirements</li> </ul>		
Patient population	Initial dose	
<b>Neonates</b>	Refer to <a href="#">Australasian Neonatal Medicines formulary (ANMF) – Tobramycin neonatal monograph</a> for dosing information. Note: Neonate on ECMO – Consider alternative antibiotic in consultation with ID. If tobramycin is essential, seek ID/ PICU expert advice on dosing and monitoring.	
<b>Infants and children with normal renal function (CrCl &gt;60 mL/min/1.73m<sup>2</sup>)</b>	<b>General infection (including Non CF bronchiectasis):</b> Adjust according to TDM. <b>More than 1 month to 10 years of age:</b> 7.5 mg/kg IV 24-hourly (Max 320 mg/day initial dose). <b>More than 10 years to 18 years of age:</b> 6 mg/kg IV 24-hourly (Max 560 mg/day initial dose).	
	<b>Critically ill/ septic shock:</b> <b>More than 1 month to 10 years of age:</b> 7.5 mg/kg IV 24-hourly (Max 320 mg/day initial dose). <b>More than 10 years to 18 years of age:</b> 7 mg/kg IV 24-hourly (Max 640 mg/day initial dose). Adjust according to TDM.	
<b>Infants and children with renal insufficiency (CrCl &lt; 60 mL/min/1.73m<sup>2</sup>)</b>	<b>Initial dose:</b> <b>More than 1 month to 18 years of age:</b> <ul style="list-style-type: none"> <li>• General infection: 5 mg/kg IV (Max 320mg)</li> <li>• Critically ill/ septic shock: 7 mg/kg IV (Max 560 mg)</li> </ul>	
	<b>Creatinine clearance (CrCl) (Modified Schwartz)</b>	<b>Initial dosing interval</b>
	<b>40 to 59 mL/min/1.73m<sup>2</sup></b>	36-hourly dosing Perform TDM. Withhold dose until trough level <1mg/L.
	<b>20 to 39 mL/min/1.73m<sup>2</sup> (including Haemodialysis, CRRT and ECMO)</b>	Consider other agents. If essential, give a single IV dose, perform TDM. Withhold dose until trough level <1mg/L. Seek ID/renal/pharmacist advice on re-dosing.
	<b>Less than 20 mL/min/1.73m<sup>2</sup></b>	Avoid. Seek ID specialist advice.
<b>Cystic fibrosis</b>	<b>No risk factors present:</b> >1 month of age to 18 years of age: 10 mg/kg IV 24-hourly (Max 660mg as initial dose) if no risk factors. Adjust according to TDM results <b>If risk factors present:</b> >1 month to 10 years of age: 10 mg/kg IV as a single dose (Max 660mg as initial dose). Adjust according to TDM. >10 years to 18 years of age: 7.5 mg/kg IV as a single dose (Max 660mg as initial dose). Adjust according to TDM.  <b>If &gt;14 days IV Tobramycin required</b> – consider switching to inhaled Tobramycin 300mg twice daily to minimize risk of systemic toxicity	

**Table 3: Dosing Guidance for initiating intravenous AMIKACIN**

<b>Table 3: Dosing Guidance for initiating intravenous AMIKACIN</b>									
<b>Before starting:</b>									
<ul style="list-style-type: none"> <li>• Perform baseline CHEM20 (Urea, Creatinine, Liver function tests, electrolytes)</li> <li>• Obesity: Patients with a BMI &gt;95<sup>th</sup> centile for age – Calculate Amikacin dose based on Adjusted Body weight</li> <li>• Assess renal function and risk factors</li> <li>• Assess risk factors for ototoxicity and determine audiology screening requirements</li> </ul>									
<b>Patient population</b>	<b>Initial dose</b>								
<b>Neonates</b>	Refer to <a href="#">Australasian Neonatal Medicines formulary (ANMF) – Amikacin neonatal monograph</a> for dosing information. Note: Neonate on ECMO – Consider alternative antibiotic in consultation with ID. If amikacin is essential, seek ID/ PICU expert advice on dosing and monitoring.								
<b>Infants and children with normal renal function (CrCl &gt;60 mL/min/1.73m<sup>2</sup>)</b>	<p><b>Severe infection or Gram negative bacteraemia:</b></p> <p><b>More than 1 month to 10 years of age:</b> 22.5 mg/kg IV 24-hourly (Max 1500 mg/day initial dose).</p> <p><b>More than 10 years to 18 years of age:</b> 18 mg/kg IV 24-hourly (Max 1500 mg/day initial dose).</p> <p>Adjust according to TDM.</p>								
<b>Infants and children with renal insufficiency (CrCl &lt; 60 mL/min/1.73m<sup>2</sup>)</b>	<p><b>Severe infection or Gram negative bacteraemia:</b></p> <p><b>More than 1 month to 10 years of age:</b> 22.5 mg/kg IV (Max 1500 mg) as initial dose</p> <p><b>More than 10 years to 18 years of age:</b> 18 mg/kg IV (Max 1500 mg) as initial dose</p>								
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<b>Less than 20 mL/min/1.73m<sup>2</sup></b>	Avoid. Seek ID specialist advice.								
<b>Cystic fibrosis</b>	<p><b>Non-tuberculous mycobacterium infections:</b></p> <p><b>More than 1 month to 10 years of age:</b> 30 mg/kg IV 24-hourly (Max 1500 mg/day initial dose).</p> <p><b>More than 10 years to 18 years of age:</b> 15 mg/kg IV 24-hourly (Max 1500 mg/day initial dose).</p> <p>Adjust according to TDM.</p>								

## Administration Instructions

### Reconstitution/Dilution, Route and Method of Administration

- Gentamicin/ tobramycin – it is recommended that dose is made up to 30 mL with sodium chloride 0.9 % and infused over 30 minutes via syringe driver.
- Smaller volumes may be required in neonates or patients who are fluid restricted. Refer to Paediatric injectable guidelines – [Gentamicin](#) or [Tobramycin](#) monograph for more information.
- Amikacin - refer to Paediatric injectable guidelines – [Amikacin](#) monograph.
- The following information is critical to the accuracy of Area Under the Curve (AUC) monitoring and should be [documented in the electronic medical record \(ieMR/ Metavision\)](#) for each dose administered:
  - Infusion start time
  - Infusion finish time (the time the IV flush is connected)
  - If IV line was primed with sodium chloride 0.9% or drug
  - Mode of administration (burette or syringe driver)

## Clinical Considerations

### Adverse Reactions

#### Ototoxicity and nephrotoxicity

- See 'Precautions'

#### Extravasation risk

Intravenous amikacin, gentamicin or tobramycin is considered low risk for phlebitis or extravasation. If the infusion “tissues”, the skin around the infusion site is red or the patient indicates any pain or discomfort, suspend the infusion and seek immediate medical review. Print [CHQ-PROC-60579 Extravasation and Infiltration](#) and follow the instructions for medical review and the subsequent recommendations for management. Seek specialised clinical review even if the injury looks minor.

# Therapeutic Drug Monitoring

## General principles

- Appropriate monitoring during therapy includes assessment of both:
  - Serum drug levels (TDM) if indicated. Monitoring of drug levels should not replace careful clinical monitoring and adjustment of therapy
  - Clinical outcomes for toxicity (renal function, audiology testing, assessment of vestibular function) and efficacy (i.e., resolution of infection)
- Aminoglycosides exhibit concentration dependent kinetics, with once daily administration (extended interval dosing) is ideal to achieve optimal C<sub>max</sub> (peak concentration) levels approaching 8 to 10 times the Minimum inhibitory concentration (MIC) for the micro-organism.
- Multiple daily dosing is reserved for specific clinical indications where synergism between aminoglycoside and beta-lactam antimicrobials are required to achieve clinical cure (e.g., enterococcal or streptococcal endocarditis). Higher risk of renal toxicity has been observed with multiple daily dosing regimens.
- Aminoglycosides are hydrophilic antibiotics. Significant changes in Volume of distribution (V<sub>d</sub>) and renal clearance (CL) can impact on overall drug exposure. This highlights the importance of TDM, especially Area-Under-The-Curve (AUC) monitoring in patients with critical illness including sepsis, burns, cystic fibrosis and renal impairment.
- Amikacin, gentamicin and tobramycin samples are analysed using Atellica® immunoassay by Pathology Queensland.
  - It is important to note that variability in results have been reported between different immunoassays
  - Results reported via the Beckman® versus Atellica® immunoassays cannot be used interchangeably.

## No therapeutic drug monitoring

- Therapeutic drug monitoring is not required for patients over 1 month of age receiving less than 72 hours of intravenous aminoglycoside therapy, who are also:
  - haemodynamically stable
  - with normal renal function
  - With no underlying renal disease
  - without concomitant nephrotoxic or ototoxic agents
  - not at extremes of weight
- Patients with risk factors receiving intravenous aminoglycosides should have TDM performed (Table 4 and 5).

## Trough level monitoring

- Trough level monitoring of aminoglycosides is for safety, to detect accumulation and potential for toxicity.
  - Timing of level – 30 minutes before dose
- It is not recommended to utilise trough levels with nomograms to adjust aminoglycoside doses in paediatrics. AUC monitoring should be used for patients requiring optimization of aminoglycoside treatment.



- Refer to Table 4 and 5 for guidance on timing of levels, TDM targets and additional considerations.

### Area Under the Curve (AUC) monitoring

AUC monitoring can be performed using a Bayesian forecasting or log-linear regression method with two paired serum samples. Both methods allow prediction of the C<sub>max</sub>, AUC and C<sub>min</sub> (C<sub>24</sub>) for a specific dosing interval.

**Unless a health service has access to Bayesian calculator with validated paediatric population pharmacokinetic models and expertise with AUC monitoring, it is recommended that the log-linear method is used to guide dosing.**

### Log-linear regression method<sup>14</sup>

The [Queensland Children's Hospital – Area Under the Curve calculator](#) is available via the Children's Health Queensland Antimicrobial stewardship website for Queensland Health clinicians.

Log-linear methods utilise a one compartment model to predict target attainment – seek specialist/pharmacist advice on interpretation of results in patients where delayed renal clearance is a concern or renal risk factors are present.

Please contact the CHQ AMS Pharmacist or QCH Pharmacy department for more information on training and support for clinicians who would like to utilise the AUC calculation tool.

### Data entry

Interpretation of the plasma drug levels require knowledge of patient's condition, risk factors, weight, height, serum creatinine, drug dose, exact time of commencement and end of infusion (including mode of administration) and exact times of blood collections.

Accuracy of data entry is critical to ensure calculations are performed correctly.

### Timing of levels

- 2 hour post dose level – timed from start of infusion
  - Ideal collection window: Within 90 minutes to 2.5 hours from start of infusion
- 6 hour post dose level – timed from start of infusion
  - Ideal collection window: Within 6 to 8 hours from start of infusion

### Time adjustment

In patients receiving the intravenous aminoglycoside dose via a burette, if the line is primed with sodium chloride 0.9% (not drug), there is a time adjustment to the infusion start and finish time required.

Documented infusion start time: 6:00 am

Documented infusion finish time: 6:30 am

- Aminoglycoside infusion volume: 30 mL
- Infusion rate: 60 mL/hour
- Administered via Burette, line primed with sodium chloride 0.9% (Burette giving set volume: 20 mL)

Calculated time to deliver line priming volume, before drug reaches patient: 20 minutes

Time to enter into AUC calculator:

- Actual infusion start time: 6:20 am
- Actual infusion finish time: 6:50 am

## Therapeutic targets and timing of levels for intravenous aminoglycosides

Table 4: Aminoglycoside Therapeutic drug monitoring targets		
Indication	TDM target	Timing of level
<b>Gentamicin</b>		
Urinary tract infection	True trough <1mg/L	Trough level 30 minutes pre-dose on day 2 or 3 of therapy. Generally uncomplicated UTI requires less than 72 hours of treatment. Consider early IV to oral switch in clinically stable patients without bacteraemia/ serious infection.
Streptococcal or enterococcal endocarditis	True trough <1mg/L	Trough level 30 minutes pre-4 <sup>th</sup> dose on day 2  Repeat level every 48 to 72 hours based on risk factors
Febrile neutropenia, Septic shock, Gram negative bacteraemia with MIC 2 mg/L (excl. <i>Pseudomonas aeruginosa</i> )	Cmax 16 to 20 mg/L Cmin < 1mg/L AUC 80 to 100	Perform AUC monitoring (2 and 6 hour post dose level) on day 1 or 2 of therapy.  Repeat level every 48 to 72 hours based on risk factors or when dose is adjusted.
<b>Directed therapy:</b> Minimum inhibitory concentration (MIC) for micro-organism cultured may inform Cmax target to ensure therapeutic efficacy. Seek ID specialist/AMS pharmacist advice.		
<b>Tobramycin</b>		
<i>Pseudomonas aeruginosa</i> bacteraemia	Cmax 25 to 40 mg/L Cmin < 1mg/L AUC 80 to 100	Perform AUC monitoring (2 and 6 hour post dose level) on day 1 or 2 of therapy.  Repeat level every 48 to 72 hours based on risk factors or when dose is adjusted.
Pulmonary exacerbation with CF or Non-CF bronchiectasis	See Tables 4 and 5	
<b>Amikacin</b>		
Non-tuberculous mycobacterial infection	Cmax 80 to 100 mg/L Cmin <5mg/L No AUC target	Perform AUC monitoring (2 and 6 hour post dose level) on day 1 or 2 of therapy.  Repeat level every 48 to 72 hours based on risk factors or when dose is adjusted.
<i>Pseudomonas aeruginosa</i> bacteraemia	Cmax 60 to 80 mg/L Cmin < 5mg/L No AUC target	Perform AUC monitoring (2 and 6 hour post dose level) on day 1 or 2 of therapy.  Repeat level every 48 to 72 hours based on risk factors or when dose is adjusted.
<b>Amikacin, Gentamicin and Tobramycin</b>		
Patients with risk factors* present	Target as per indication above	AUC monitoring on day 1 of therapy. Take 2 and 6 hr post dose level and true trough level (taken at 23.5 hrs post 1 <sup>st</sup> dose) to ensure dose is cleared within 24 hours.  Withhold 2 <sup>nd</sup> dose until true trough level is less than specified trough for agent (tobramycin and gentamicin <1mg/L; amikacin <5mg/L) and the results have been reviewed by Treating team/Pharmacist.

**Table 5: Therapeutic targets and timing of levels for intravenous Tobramycin in patients with Cystic fibrosis and Non-CF bronchiectasis**

Indication	TDM target	Timing of levels	
		Week 1	Week 2
<b>Infective exacerbation - Pseudomonas aeruginosa negative</b>	Cmax 20 to 35 mg/L No AUC target Cmin (C24) < 1 mg/L	Day 2 of therapy (if admitted on a Friday, levels on Monday = day 4) Initial AUC – 2 and 6 hr post dose levels  Repeat levels after dose adjustment is made. Baseline CHEM20.	True trough level taken 30 minutes pre-dose (level can be taken between days 6 to 8 of course) Repeat CHEM20.
<b>Eradication – Pseudomonas aeruginosa</b>	Cmax 25 to 40 mg/L AUC 90 – 120 Cmin (C24) < 1 mg/L	Day 2 of therapy Initial AUC – 2 and 6 hr post dose levels  Repeat levels after dose adjustment is made. Baseline CHEM20.	Day 6 to 8 Repeat AUC – 2 and 6 hr post dose levels  Repeat levels after dose adjustment is made. Repeat CHEM20.
<b>Infective exacerbation - Chronically colonised with Pseudomonas aeruginosa</b>	Cmax 25 to 40 mg/L Cmin (C24) < 1 mg/L If poor clinical response, target AUC 90 - 120	Day 2 of therapy (if admitted on a Friday, levels on Monday = day 4) Initial AUC – 2 and 6 hr post dose levels  Repeat levels after dose adjustment is made. Baseline CHEM20.	True trough level taken 30 minutes pre-dose (level can be taken between days 6 to 8 of course)  Repeat CHEM20.  Consider AUC monitoring if poor clinical response from baseline observed (e.g., cough, spirometry)
<b>Patients with risk factors present*</b>	Target as per indication above	Day 1 of therapy- Initial AUC – 2 and 6 hr post dose levels and true trough level (taken at 23.5 hrs post 1 <sup>st</sup> dose) to ensure dose is cleared within 24 hours.  Withhold 2 <sup>nd</sup> dose until true trough level is less than 1mg/L and the results have been reviewed by Respiratory Specialist and Pharmacist.  Repeat levels after dose adjustment is made. Once dose is optimized, repeat levels every 48 to 72 hours based on clinical progress.	
<p><b>Notes:</b> Do not exceed maximum dose of tobramycin IV 15mg/kg/day. Consult Respiratory and ID/AMS specialist for advice on alternative treatment choice.</p> <p>Consider audiometry testing in patients with risk factors (including Pre-existing hearing impairment, at risk of tobramycin accumulation, prolonged course &gt;14 days)</p> <p><b>HITH</b> – Tobramycin 2 hour post dose level and 6 hour level at clinic appointment or local QH hospital (noting: samples will be transferred to closest central lab). Trough level will be collected by CHQ@Home</p>			

## Additional Information

### Electronic prescribing in ieMR

Prescriber to use Paediatric [Tobramycin](#) or [Gentamicin](#) Power Plan to prescribe and order first level/s by placing an electronic pathology order. For amikacin prescribing, utilise the dosing guidance in this guideline to prescribe and order pathology in ieMR.

The prescriber or pharmacist should also place a '[Medication Level placeholder](#)' which will appear on the Medication Administration Record (MAR) - this acts as a task reminder to the nursing staff when a medication level is due to ensure optimal collection time.

Take amikacin, gentamicin or tobramycin level/s as specified and then withhold the next dose until the level returns and is reviewed by the Treating team and/or Pharmacist.

### Documenting therapeutic drug monitoring results and plan

Prescriber or Pharmacist to document an Aminoglycoside Therapeutic drug monitoring (TDM) note in the patient's electronic medical record with details on interpretation of results and recommendation for dose adjustment/further monitoring.

Example of tobramycin TDM note template below:

<p><b>Tobramycin Therapeutic drug monitoring – note</b></p> <p>Indication for treatment: _____</p> <ul style="list-style-type: none"> <li>• Day of therapy = _____</li> <li>• Intended duration of treatment (if known) = _____</li> <li>• Current IV dose and frequency = _____             <ul style="list-style-type: none"> <li>○ Infusion start time</li> <li>○ Infusion finish time</li> <li>○ Line primed with: (drug/sodium chloride 0.9%)</li> <li>○ Mode of administration: (syringe driver/ burette)</li> </ul> </li> </ul> <p>Current renal function: _____</p> <p>Risk factors (see guideline and specify)</p> <p>Relevant microbiology results:</p> <p>Tobramycin therapeutic target (see guideline and specify which target is used)</p> <ul style="list-style-type: none"> <li>• Cmax</li> <li>• Cmin</li> <li>• AUC</li> </ul> <p>Tobramycin TDM results:</p> <ul style="list-style-type: none"> <li>• 2 hour level (date/time and result)</li> <li>• 6 hour level (date/time and result)</li> <li>• Trough level (date/time and result)</li> <li>• Sample taken from (specify - finger prick, heel prick, venepuncture, CVAD)</li> </ul> <p>Tobramycin AUC calculation (screenshot or specify Cmax, AUC and Cmin results)</p> <p>Interpretation of results: _____</p> <p>Recommendations: _____</p> <p>Discussed with (specify) _____</p> <p>Handover provided to (specify) _____</p> <p><b>Reviewed by:</b> _____ <b>Signature</b> _____</p>	
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## Supporting documents

### Procedures, Guidelines and Protocols

- CHQ-PROC-01036 [Antimicrobial: Prescribing and Management](#)
- CHQ [Antimicrobial restrictions](#)
- CHQ-PROC-01001 [Medication – Prescribing](#)
- CHQ-PROC-01039 [Medication- Administration](#)
- CHQ [High Risk Medication List](#)
- CHQ-PROC-60579 – [Extravasation and Infiltration](#)

## Consultation

Key stakeholders who reviewed this version:

- Pharmacist Advanced – Antimicrobial Stewardship
- Director – Infection Management and Prevention service (IMPS)
- Paediatric Respiratory Consultant
- Paediatric Nephrologist
- Paediatric Oncologist
- Paediatric Intensivist
- Director of Pharmacy
- Director of Audiology
- Pharmacist Lead – Oncology
- Pharmacist Lead – Medical
- Senior Clinical pharmacist - PICU
- Pharmacist Lead – Surgical
- Senior Clinical Pharmacist – Cystic fibrosis
- CHQ Medicines Advisory Committee 24/02/2023

## References and suggested reading

1. Rizk HG, Lee JA, Liu YF et al. Drug-Induced Ototoxicity: A Comprehensive Review and Reference Guide. *Pharmacotherapy* 2020;40(12):1265–1275. doi: 10.1002/phar.2478
2. Children’s Health Queensland and Health Service Work instruction CHQ-WI-00171. Audiology- Oncology Ototoxic Monitoring. Available online: [https://qheps.health.qld.gov.au/\\_data/assets/pdf\\_file/0033/25753338/wi-00171.pdf](https://qheps.health.qld.gov.au/_data/assets/pdf_file/0033/25753338/wi-00171.pdf)
3. Schwartz GJ and Work DF. Measurement and estimation of GFR in children and adolescents. *J Am Soc Nephrol.* 2009; 4(11): 1832-643
4. Principles of Aminoglycoside Use [published 2019 Apr. Updated 2021 Aug]. In: eTG complete [digital]. Melbourne: Therapeutic Guidelines Limited; 2019 Apr. Available from: <https://www.tg.org.au>

5. Australian Medicines Handbook: Children's Dosing Companion. 2023. Available online: <https://childrens.amh.net.au/> [Accessed 31 Jan 2023]
6. Amikacin Drug information. UpToDate. Waltham, MA: UpToDate Inc. Available from: <http://www.uptodate.com> . [Accessed on January 31, 2023]
7. Gentamicin Drug information. UpToDate. Waltham, MA: UpToDate Inc. Available from: <http://www.uptodate.com> . [Accessed on January 31, 2023]
8. Tobramycin Drug information. UpToDate. Waltham, MA: UpToDate Inc. Available from: <http://www.uptodate.com> . [Accessed on January 31, 2023]
9. Plover C. Paediatric Injectable Guidelines. 2021 Ed. Flemington, Vic: The Royal Children's Hospital; 2020 [Internet] [cited 2023; Jan] Available from: <https://piq.rch.org.au/>
10. Australasian Neonatal Medicines Formulary (ANMF) Consensus Group. Newborn Care Centre Clinical resources – Medications. Neomed Formularies. [Internet] Sydney, NSW [cited 2023, Jan]; Available from: <https://www.anmfonline.org/clinical-resources/>
11. Sydney Children's hospital. Aminoglycoside therapy – Paediatric Practice Guideline. Guideline No: 2012-7008-01 v4 Jan 2021. Available from: [https://www.schn.health.nsw.gov.au/\\_policies/pdf/2012-7008.pdf](https://www.schn.health.nsw.gov.au/_policies/pdf/2012-7008.pdf)
12. Abdul-Aziz MH, Alffenaar JWC, Bassetti M et al .Antimicrobial therapeutic drug monitoring in critically ill adult patients: a Position Paper. Intensive Care Med (2020) 46:1127–1153
13. Landmesser KB, Autry EB, Gardner BM et al. Comparison of the predictive value of area under the curve versus maximum serum concentration of intravenous tobramycin in cystic fibrosis patients treated for an acute pulmonary exacerbation. Pediatric Pulmonology. 2021;56:3209–3216
14. Begg E, Barclay ML, Duffull SB. A suggested approach to once-daily aminoglycoside dosing. Br J Clin Pharmacol. 1995 Jun; 39(6): 605–609.
15. Llano-Paez C, Staatz C, Lawson R et al. Differences in the Pharmacokinetics of Gentamicin between Oncology and Non-oncology Pediatric Patients. AAC. 2020; 64 (2): e01730-19
16. Tu, Q, Cotta M, Raman S et al. Individualized precision dosing approaches to optimize antimicrobial therapy in pediatric populations, Expert Review of Clinical Pharmacology, 2021; 14 (11): 1383-1399,

## Revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by
1.0 03/2020	Pharmacist Advanced – Antimicrobial Stewardship	CHQ Medicines Advisory committee	Executive Director Clinical services
2.0 24/02/2023	Pharmacist Advanced – Antimicrobial Stewardship	Director of Pharmacy	Executive Director Medical services

<b>Keywords</b>	Intravenous aminoglycoside, amikacin, gentamicin, tobramycin, nephrotoxicity, ototoxicity, TDM, therapeutic drug monitoring, trough level, AUC, area-under-the-curve, antimicrobial stewardship, 01294
<b>Accreditation references</b>	NSQHS Standards (1-8): 4 – Medication Safety, 3- Healthcare associated infections and Antimicrobial stewardship ISO 9001:2015 Quality Management Systems: (4-10)