**Canberra Hospital and Health Services**

**Guideline**

**Gentamicin - Clinical Guidelines for Dosing and Monitoring of Once Daily Gentamicin in Paediatric Patients**

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| Guideline Statement |

## Background

Gentamicin use is indicated in the management of suspected or proven gram-negative bacterial infections. Due to concerns about nephrotoxicity and ototoxicity, its use should be limited to three doses (within 48 hours duration) wherever possible.

The pharmacodynamic properties of gentamicin make once daily administration preferable to the traditional divided doses approach of giving aminoglycosides (e.g. three times daily dosing) in most children.

## Key Objective

To ensure the safe prescribing, administration and therapeutic drug monitoring of the aminoglycoside antimicrobial gentamicin, in 0–16-year-old patients for the treatment of infection at Canberra Health Services (CHS).

## Alerts

Despite monitoring and maintaining gentamicin levels within an accepted range (when drug monitoring is indicated), it is possible, although uncommon, for toxicity to occur. The most reliable way to prevent gentamicin toxicity is to minimise its use. Patients with risk factors for toxicity should have therapeutic drug monitoring (TDM).

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| Scope |

The document applies to CHS staff working within their scope of practice that prescribe, administer, monitor or advise on the use of once daily gentamicin in paediatric patients at CHS.

This procedure does not apply to:

* Adults: Refer to *Intravenous Dosing and Monitoring of Aminoglycosides in Adults*
* Patients admitted to the Neonatal Intensive Care Unit or Special Care Nursery
* Greater frequency than once daily dosing, e.g. treatment of bacterial endocarditis- seek advice from Infectious Diseases.
* Routes of administration other than intravenous (IV) or intramuscular (IM) e.g. intra-peritoneal, oral or inhaled gentamicin
* Patients with Cystic Fibrosis- seek advice from their Respiratory Specialist

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| Section 1 – Indications, Contraindications and Precautions |

## Indications

* Empiric treatment of severe gram-negative infections (recommended maximum treatment 48 hours, 3 doses)
* Other serious infections due to sensitive organisms that are resistant to other antimicrobials
* Surgical prophylaxis per [Therapeutic Guidelines: Antibiotic](https://tgldcdp.tg.org.au/viewTopic?topicfile=aminoglycoside-use-principles&guidelineName=Antibiotic#toc_d1e1481)

## Contraindications

* Allergy to aminoglycosides
* Personal or family history of deafness caused by aminoglycosides
* Myasthenia gravis (due to risk of neuromuscular blockade)

## Precautions

* Renal Impairment. A paediatric nephrologist or paediatric infectious diseases physician should be consulted in the following situations as the gentamicin dose may need to be decreased:
* A child ≤ 1yo with an elevated creatinine
* A child > 2yo with an estimated Glomerular Filtration Rate (eGFR) less than 50mL/min/1.73m2

**Note 1**: Schwartz Formula

eGFR (mL/min/1.73m2 ) = (36.5 x height (cm)) / serum creatinine (micromol/L)

* Pre-existing hearing impairment
* Neuromuscular disease
* Obesity- dose adjustment required (see Section 3- Prescribing the Initial Dose)
* Concurrent or recent administration of potentially nephro- or ototoxic medications:
* Nephrotoxic agents include furosemide, vancomycin, amphotericin, cisplatin, other aminoglycosides, aciclovir, regular use of NSAIDs
* Ototoxic agents include cisplatin and other aminoglycosides
* Repeated courses of aminoglycosides (e.g. in preceding 6 months)
* Previous aminoglycoside-induced toxicity

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| Section 2 – Restrictions |

* Gentamicin is an “ORANGE” restricted antimicrobial (as per*: Antimicrobial Stewardship procedure).*
* If Gentamicin is required beyond 48 hours (i.e. 3 doses), an application for Antimicrobial Stewardship (AMS) approval must be requested. For instructions on seeking AMS approval, refer to the *Antimicrobial Stewardship procedure.*

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| Section 3 – Prescribing the Initial Dose |

* Gentamicin can be given via the intramuscular route in the absence of intravenous access.
* Assess baseline renal function by collecting serum for urea and creatinine. Do NOT delay the initial dose in an unwell child, however, whilst waiting for the result.
* Dose reduction is required in children with obesity (BMI ≥ 95th percentile for age) because gentamicin distributes minimally in adipose tissue. Doses should be calculated based on the Adjusted body weight formula using both the Ideal Body Weight (IBW) and Measured Weight.

*Adjusted body weight = IBW^ + 0.4 X (Measured Weight - IBW)*

^IBW can be calculated by plotting the child’s weight for age on the same percentile as their height for age

**Table 1: STANDARD INITIAL DOSING**

|  |  |  |  |
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| Age | Dose (IV or IM) | Max Dose | Frequency |
| Birth (at term)\* –  < 1 month | 5mg/kg/dose | Maximum 5mg/kg/dose | 24 hourly |
| 1 month - < 10 years old | 7.5mg/kg/dose | 320mg | 24 hourly |
| 10 years and older | 6mg/kg/dose  7mg/kg/dose if septic shock or requiring ICU support | 560mg# | 24 hourly |

\* Management for preterm neonates should be discussed with NICU.

# This dose cap does not apply to critically ill children with severe sepsis or septic shock.

**Table 2: DOSING RECOMMENDATIONS FOR RENAL IMPAIRMENT**

(Less nephrotoxic agents should be used in place of gentamicin where possible. If gentamicin is used, suggest discussing with a Paediatric Renal Specialist prior to starting or as soon as possible during treatment)

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| Age | eGFR\* | Gentamicin Dose | Frequency |
| Neonate (< 1 month) | Aim to use an alternative antibiotic- discuss with Paediatrician | | |
| 1 month – 16 years | >50mL/min/1.73m2 | Standard, see Table 1 above. | |
| 30-50 mL/min/1.73m2 | 2.5 mg/kg/dose | 12 hourly |
| 10-29 mL/min/1.73m2 | 2.5 mg/kg/dose | 24 hourly |
| <10 mL/min/1.73m2 | 2.5 mg/kg/dose | 48-72 hourly |

\*Use of the Schwartz formula for calculation of eGFR is recommended. See Note 1, section 1 above.

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| Section 4 – Therapeutic Drug Monitoring (TDM) |

No TDM is necessary for:

* An otherwise healthy child or oncology patient, if treatment is planned for up to 3 doses (48hrs treatment) only; and
  + Renal function is normal at baseline and during treatment if checked
  + No concurrent nephrotoxic or ototoxic drugs are prescribed
  + Child is not obese
  + Child is not critically unwell
  + Child has no other risk factors for toxicity (see Precautions list, section 1 above)
  + Oncology patients may have a plan to give or avoid gentamicin for management of fever or febrile neutropenia documented in their management plan.

**Table 3: TDM INDICATIONS AND METHODS**

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| --- | --- | --- | --- | --- |
| Indication | Clinical considerations | Level | Target trough Level | Frequency of Monitoring |
| Infant (1 month or older) or child in whom treatment is required beyond 48hrs and renal function is normal | Review use, try to cease or switch agent or seek Infectious Disease (ID) advice | Trough level\* before 4th dose | <1mg/L | Every 3 days, more often if risk of rapid renal function change (eg. septic or critically ill patient) |
| Neonate (<1 month old) in whom treatment required for >48hrs and normal renal function | Review use, try to cease or switch agent or seek ID advice | At 22 hours after the second dose | See Table 4 below |  |
| Renal impairment or unstable renal function at any age | Review use, try to cease or switch agent or seek ID advice | Trough level before every dose | Discuss with renal specialist- usually <1mg/L if receiving once daily dosing, <2mg/L if receiving multiple daily dosing | Before every dose while renal function impaired |

\*Trough levels should be taken 30mins prior to the next dose being due.

**Table 4: NEONATAL (AGED <1 MONTH) MONITORING IF SUSPECTED TO REQUIRE >48HRS OF TREATMENT**

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| Gentamicin level (22 hours post dose) | Dosing Interval |
| ≤ 1.2 mg/L | Every 24 hours after previous dose |
| 1.3 mg/L ─ 2.6 mg/L | Every 36 hours after previous dose |
| 2.7 mg/L ─ 3.5 mg/L | Every 48 hours after previous dose |
| ≥ 3.6 mg/L | Hold dose, repeat concentration at 24 hours |

**Management of a High Trough Level**

For any patient, if the gentamicin trough level is high, discuss need for ongoing therapy with the treating Paediatrician or Infectious Diseases Specialist, and check renal function.

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| Section 5 – Incompatibilities and Interactions |

* Aminoglycosides have many incompatibilities, so should not be mixed with other drugs. For more information on specific drug incompatibilities refer to the [Australian Injectable Drugs Handbook](http://aidh.hcn.com.au/browse/g/gentamicin) (6th edition).
* Aminoglycosides are inactivated by penicillins, cephalosporins and teicoplanin so these drugs should not be administered simultaneously. It is preferable to separate doses by one hour. If it is not possible to separate doses by one hour, administer the gentamicin first, flushing the line well with a compatible fluid before and after giving each medicine.
* Avoid concurrent administration with other nephrotoxic drugs.
* Potent diuretics such as furosemide may contribute to ototoxicity and nephrotoxicity and may also cause alterations in serum and tissue concentrations.
* The neuromuscular blocking activity of some drugs, such as anaesthetic agents or opioid analgesics may be enhanced.
* For more information on specific drug interactions contact Medicines Information extension 43333.

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| Section 6 – Adverse Effects |

**Nephrotoxicity** (usually reversible)

* May present as worsening of renal function; increasing serum creatinine and proteinuria or may present as acute tubular necrosis.
* More common in patients with pre-existing renal impairment.
* In vitro, once daily dosing results in lower renal cortical concentrations compared to continuous infusions or traditional dosing and it is therefore hypothesised that once daily dosing may lessen nephrotoxicity.
* If nephrotoxicity occurs at any time, consider switching to an alternative antimicrobial therapy.

**Hearing and Vestibular toxicity**

* Ototoxicity and vestibular toxicity is irreversible in approximately 50% of cases. If developing, gentamicin should usually be stopped, and alternatives considered.
* Aminoglycosides affect both cochlear and vestibular function, with high frequency hearing usually affected before low frequency hearing.
* May present as nausea, vertigo or tinnitus.
* Testing of hearing and vestibular function should be done for patients receiving gentamicin for longer than 5 days, and repeat periodically if therapy is continued for more than 14 days. Signs of vestibular dysfunction include nystagmus, ataxia and a positive Romberg’s sign.

**Reporting**

Adverse outcomes must be:

* Recorded in the patient’s clinical record
* Reported by the medical team using the electronic Adverse Drug Reaction (ADR) reporting form (located on CHS Health Hub → Clinical Apps → Adverse Drug Reactions)
* Clearly documented in the patient’s discharge summary and discussed with the patient or their family.

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| Evaluation |

**Outcomes**

* Safe prescribing, administration and therapeutic drug monitoring of gentamicin.
* Prevention of gentamicin toxicity (renal, hearing and vestibular impairment).

**Measures**

* Adverse Drug Reactions (ADRs) to the use of gentamicin must be reported via the electronic ADR reporting form for investigation by the Adverse Drug Reaction Reporting Committee.
* Any errors with gentamicin prescribing or administration should be reported in RiskMan and reviewed at Paediatric RiskMan meetings monthly, and if required, escalated to Departmental Quality and Safety Meetings, to identify trends, guideline deviation and establish recommendations for quality improvement.
* Serious adverse events may be referred to the Clinical Review Committee via the Quality and Safety or Paediatric Morbidity and Mortality meetings for investigation.

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| Related Policies, Procedures, Guidelines and Legislation |

**Policies**

* Nursing and Midwifery Board of Australia (NMBA) Requirements for Practice
* Medication Handling Policy

**Procedures**

* Intravenous Dosing and Monitoring of Aminoglycosides in Adults
* Patient Identification and Procedure Matching
* Antimicrobial Stewardship
* Infection Prevention Control and Healthcare Associated Infections

**Guidelines**

* Neonatal Intensive Care Drug Manual

**Legislation**

*Health Records (Privacy and Access) Act* 1997

*Human Rights Act* 2004

*Work Health and Safety Act* 2011

**Other**

Australian Charter of Health Care Rights

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| References |

1. Clinical Excellence Commission (2017) Safe Gentamicin Prescribing in Paediatrics available at <https://www.cec.health.nsw.gov.au/keep-patients-safe/medication-safety/high-risk-medicines/Gentamicin-paediatric>.
2. Aminoglycoside Therapy- SCH Practice Guideline 2021
3. Aminoglycoside Dosing and Monitoring- CHW Practice Guideline 2021 <http://www.schn.health.nsw.gov.au/_policies/pdf/2011-8018.pdf>
4. Australian Medicines Handbook; Children’s Dosing Companion (July 2021) Gentamicin available at <https://childrens.amh.net.au/monographs/gentamicin>
5. Kids Cancer Centre, Sydney Children’s Hospital Randwick (2017) Supportive Management Information for Medical and Nursing Staff.
6. Australian Injectable Drugs Handbook 8th Edition (Oct 2021) [AIDH - GENTAMICIN (hcn.com.au)](https://aidh.hcn.com.au/browse/g/gentamicin)

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| Definition of Terms |

**Romberg’s sign**: Romberg's sign is a test used in an exam of neurological function for balance.

**Nephrotoxicity**: The quality of being toxic to kidney cells.

**Ototoxicity:** The property of being injurious to the functions of the ear.

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| Search Terms |

Gentamicin, Paediatric gentamicin, Gentamicin dosing, Gentamicin monitoring, Gentamicin level

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| Attachments |

*These could include any supporting information that would be useful to staff such as information sheets or flow charts*

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*Policy Team ONLY to complete the following:*

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| --- | --- | --- | --- |
| *Date Amended* | *Section Amended* | *Divisional Approval* | *Final Approval* |
| *16/02/2022* | *Complete Review* | *Susan Freiberg, ED-WY&C* | *CHS Policy Committee* |
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*This document supersedes the following:*

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| *Document Number* | *Document Name* |
| *CHHS18/169* | *Gentamicin - Clinical Guidelines for Dosing and Monitoring of Once Daily Gentamicin in Paediatric Patients* |