Specialised Medication – Intravenous Aminoglycosides for ADULT Non-Pregnant Patients Guideline

1. Guiding Principles

For Paediatric patients, refer to the Perth Children Hospital ChAMP Monographs

For Neonatal patients, refer to the King Edward Memorial Hospital and Perth Children's Hospital Neonatology Medication Protocols

For Obstetric patients, refer to the Women and Newborn Health Service (KEMH) Guidelines.

Recommendation by a clinical microbiologist or Infectious Diseases Physician is required for continuation of aminoglycoside therapy beyond 72 hours duration.

If the initial intention is for greater than 72 hours of aminoglycoside therapy, then therapeutic drug monitoring (as described below (2.8.1) should be undertaken as soon as possible.

Doses in this guideline do not apply to the use of aminoglycosides in synergistic therapy (such as endocarditis), resistant *mycobacterium avium* complex infections, brucellosis or nocardiosis. Refer to therapeutic guidelines or follow the specific advice from infectious disease physician or microbiologist for these conditions.

2. Guideline

Aminoglycosides are bactericidal antibiotics and act by inhibiting protein synthesis in susceptible bacteria. Most community and healthcare associated gram negative pathogens are susceptible to aminoglycosides. Amioglycosides are rarely associated with anaphylaxis, are rarely associated with *clostridium difficile* infections and have a synergistic effect with cell wall active drugs such as beta lactams and glycopeptides. Their use is limited by nephrotoxicity (usually reversible) and vestibular or auditory toxicity (usually irreversible).[3]

2.1 Presentation[1]

Amikacin: 500mg in 2mL
Gentamicin: 80mg in 2mL
Tobramycin: 80mg in 2mL

2.2 Indication[2,3]

Empirical treatment for 48 hours or less for suspected or proven gram negative sepsis
Surgical prophylaxis (WATAG Surgical Prophylaxis Guidelines).

Low doses as synergistic treatment of serious systemic enterococcal infections (with a beta-lactam or vancomycin).

Directed therapy to treat infections where resistance to safer antimicrobials has been shown or as combination therapy to treat serious Pseudomonas aeruginosa infection or brucellosis.

2.3 Contraindications[1,3]

DO NOT use in patients with

- A history of aminoglycoside induced vestibular or auditory toxicity
- Severe hypersensitivity to aminoglycosides
- Myasthenia gravis

2.4 Precautions[1,2,3]

Generally should not be used in

- pre-existing severe hearing problems or vestibular problems or family history of aminoglycoside induced auditory toxicity

Single doses can be used in

- chronic liver disease
- chronic renal failure or deteriorating renal function
- Age greater than 80 years (increased prevalence of pre-existing hearing or renal impairment).

2.5 Dosage [3,4]

Initial Dosing and subsequent dosing:

Empirical treatment:
Gentamicin and tobramycin:
Usual once daily dosage of ideal body weight up to a **maximum of 400mg**, rounded to nearest 40mg.

Creatinine clearance (mL/min)	Dose (based on ideal weight)	Dosing interval	Maximum number of empirical doses
>60	4-5 mg/kg	24 hourly	3 (at 0, 24 and 48 hours)
40 - 60	4-5 mg/kg	36 hourly	2 (at 0 and 36 hours)
< 40	4 mg/kg	Give initial dose then seek expert advice	

- Amikacin: 16-20mg/kg up to a maximum of 1500mg

For patients who are overweight or obese use ideal body weight (IBW).

Male: IBW[kg] = 50.0 + 0.91 (Ht [cm] - 152.4)

Female: IBW [kg] = 45.5 + 0.91 (Ht [cm] - 152.4)

Dose guides for obese patients are available in Therapeutic Guidelines Antibiotics

Considerations:

- Aminoglycoside administration should not be delayed to ascertain renal function. Subsequent dose or interval can be reviewed once renal function is known.
- Doses up to 7mg/kg ideal body weight (max. 560mg) of gentamicin is appropriate in critically ill patients with severe sepsis or shock. A lower dose should be used in patients with renal impairment (CrCl 40 – 60ml/min: 5 mg/kg; CrCl < 40ml/min: 4mg/kg).

Directed therapy:

- Commence therapy as above and see Therapeutic Drug Monitoring for ongoing doses (2.8.1)

Synergistic dosing for streptococcal or enterococcal infective endocarditis consult with ID Physician or clinical Microbiologist. Usual dose is 3mg/kg in a single or divided doses (1mg/kg 8 hourly)

2.6 Administration [3,5]

Gentamicin and tobramycin may be given as an IV injection. Dilute to 20ml and give as a slow IV over 5 minutes.

Gentamicin and tobramycin can be given as an intramuscular injection (maximum 4ml per site) or intravenous infusion over 30 minutes.

Amikacin should be given as an infusion over 30 minutes or intramuscular injection

Special Note [(5)]: Aminoglycosides are inactivated by penicillin and cephalosporin antibiotics.

- Do not mix in the same injection or infusion solution.
- Administer at separate sites if possible.
- In patients with normal renal function where it is not practical or possible to administer separately, flush the line well before and after giving each drug.
- In patients with renal impairment, separate the drugs by several hours.

2.7 Storage [1,5]

Store below 25 degrees C except for tobramycin preservative free (store at 2 to 8 degrees C). Protect from light

2.8 Monitoring requirements [3,4]

2.8.1 Therapeutic Drug Monitoring:

NB: Therapeutic drug monitoring is only required if treatment extends beyond 48 hours.

Methods for therapeutic drug monitoring depend on local availability and resources. Although AUC methods are best practice, the nomogram approach may still be used in some regions. Contact your Regional Pharmacy Department for local processes, support and dosing advice.

Measure the plasma concentration:

- On the first dose of **directed therapy**, then usually every 48 hours, but more frequently if renal function is unstable.
- At least twice weekly for **synergistic dosing,** but more frequently if renal function is unstable. Liaise closely with infectious Disease.

Directed therapy
The computerised AUC method (e.g. Aladdin® or TCIWorks) is more accurate requires:

- Two plasma aminoglycoside levels during each dosage interval are required to estimate a 24-hour AUC:
  - a peak level taken 30 minutes after the end of the infusion and
  - a second level taken 6-14 hours after the end of the infusion

The nomogram method requires:

- One plasma aminoglycoside level 6-14 hours after the end of the infusion

Patients with significant renal impairment should only be re-dosed when the plasma level falls to 0.5 - 1mg/L (amikacin 2-4mg/L). Therapeutic drug monitoring using computerised AUC or the nomogram method is not required. Close liaison with Infectious Disease physician or pharmacist experienced in ID is recommended.

Synergistic dosing for streptococcal or enterococcal infective endocarditis

- Trough concentrations should be measured and kept below 1mg/L. Therapeutic drug monitoring using computerised AUC or the nomogram method is **not** required. For patients with trough concentrations of >1mg/L, consideration should be given to extending the dosage interval rather than decreasing the dosage size.

2.8.2 General monitoring recommendations

- Renal function should be assessed on initiation of therapy and then every 2-3 days if treatment extends beyond 48 hours. Frequency may need to be increased if the patient's renal function is unstable.
- Baseline audiometry (if available) should be considered at the initiation of therapy in patients who are likely to be prolonged courses and repeated periodically during the course of aminoglycoside therapy.
- All patients should be informed, if possible, of the potential for vestibular and auditory toxicity, and instructed to report any balance or hearing problems, which may become apparent early in the course of treatment or weeks after therapy has stopped. In particular, patients receiving aminoglycosides should be asked regularly about:
    - gait ataxia and imbalance
    - oscillopsia (the subjective sensation of bouncing vision) or blurred vision during head movement
    - hearing loss.

There is information available about simple bedside tests that can be completed by medical staff: Clinical diagnosis of bilateral vestibular loss: three simple bedside tests.

See Therapeutic Guidelines: Principles of aminoglycoside use for additional aminoglycoside dosing and monitoring information.

3. Roles and Responsibilities

The **Medical Officer** completes all treatment and duties within scope of practice.

The **Registered Nurse** completes all nursing duties for the patient within scope of practice including escalation of care as per the MR140A WACHS Adult Observation and Response Chart.

4. Compliance

Failure to comply with this policy document may constitute a breach of the WA Health Code of Conduct (Code). The Code is part of the Employment Policy Framework issued pursuant to section 26 of the *Health Services Act 2016* (HSA) and is binding on all WACHS staff which for this purpose includes trainees, students, volunteers, researchers, contractors for service (including all visiting health professionals and agency staff) and persons delivering training or education within WACHS.

WACHS staff are reminded that compliance with all policies is mandatory.

5. Evaluation

Adverse events and clinical incidents relating to the administration of aminoglycosides are to be zero (0).

6. Standards

National Safety and Quality Healthcare Standards – 3.15, 4.1, 4.3, 4.13

7. Legislation

Medicines and Poisons Act 2014 (and Medicine and Poisons Regulations 2016)

8. References

1. eMIMs: Accessed January 2019
2. Australian Medicines Handbook: Accessed January 2019
3. eTG: Principles of aminoglycoside use. 16th Edition. 2019
4. Fiona Stanley Hospital – Guidelines for Aminoglycoside Dosing and Monitoring in Adults. Date issued: 11/2014
5. SHPA Australian Injectable Drugs Handbook. 7th Edition. Accessed May 2019

9. Related Policy Documents

WACHS Medication Administration Policy
WACHS High Risk Medications Procedure

10. Related WA Health Policies

OD 0561/14 WA High Risk Medication Policy

11. Policy Framework

Clinical Governance, Safety and Quality
Public Health Policy Framework

This document can be made available in alternative formats on request for a person with a disability

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