GENTAMICIN (SULFATE)

SCOPE (Area): FOR USE IN: All ward areas, except as outlined below
EXCLUSIONS: Paediatrics (seek Paediatrician advice)
SCOPE (Staff): Medical, Nursing and Pharmacy

BRAND NAMES
No brand names.

PHARMACOLOGY AND PHARMACOKINETICS
Gentamicin is an aminoglycoside antibiotic with a broad Gram-negative spectrum (including Pseudomonas aeruginosa) that exhibits concentration-dependent antibacterial activity. With prolonged exposure, gentamicin is nephrotoxic and ototoxic. The half-life is about 2 to 3 hours in patients with normal renal function, but prolonged in patients with impaired renal function as gentamicin is nearly 100% renally cleared.

INDICATIONS
- Empirical treatment (for up to 48 hours) of serious infections likely to be caused by a Gram-negative pathogen (e.g. urosepsis, sepsis of intra-abdominal origin).
- A single dose as surgical prophylaxis.
- Directed therapy (for longer than 48 hours- must be discussed with ID or AMS) for:
  - Infections with proven resistance to safer antibiotics.
  - Combination therapy for serious Pseudomonas aeruginosa infections or Brucellosis.
  - Synergistic treatment of Streptococcal or Enterococcal endocarditis (low doses of 1mg/kg, given 8 hourly).

CONTRAINDICATIONS
- Serious allergic reaction to any aminoglycoside (rare).
- Previous vestibular or auditory toxicity due to any aminoglycoside.
- Myasthenia gravis.

PRECAUTIONS
Aminoglycosides should generally be avoided, unless the infection is life-threatening, in patients with the conditions listed in this box:
- Pre-existing significant auditory impairment (hearing loss or tinnitus).
- Pre-existing vestibular problems (including dizziness, vertigo or balance problems).
- A family history (first-degree relative) of auditory toxicity caused by an aminoglycoside.
- Chronic renal impairment (creatinine clearance less than 40ml/min) or rapidly deteriorating renal function.
- Advanced age (80 years or older) depending on calculated creatinine clearance.
PREGNANCY AND BREASTFEEDING
Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- **Nephrotoxic drugs** - including but not limited to vancomycin, frusemide, amphotericin. Increased risk of nephrotoxicity when used in combination
- **Ototoxic drugs** - including but not limited to frusemide and cisplatin. Possibly increased risk of ototoxicity when used in combination
- **Magnesium sulfate** - additive neuromuscular blocking effects. Use combinations carefully and monitor respiratory function.
- **Non-depolarising neuromuscular blockers** - Prolonged effect and may lead to respiratory insufficiency. Reduce neuromuscular blocker dose and monitor closely.
- **Suxamethonium** - Prolonged effects of suxamethonium which may lead to respiratory insufficiency. Reduce suxamethonium dose and monitor neuromuscular blockade closely.
- **Penicillins and cephalosporins** - gentamicin is inactivated by some penicillins and should not be mixed or given simultaneously with these drugs. In renal failure administration times should be staggered by several hours, HOWEVER in septic patients administer the antibiotic which takes the least time to inject or infuse, balancing this with administering the most needed/effective antibiotic for the organism suspected of causing the sepsis. Do not delay the administration of subsequent antibiotics. See Australian Drugs Injectable Handbook for further information.

See Appendix 2 for further details and additional potential drug interactions

DOSAGE AND ADMINISTRATION

Empirical therapy

Short term empirical therapy is the primary indication for aminoglycosides pending the result of investigations and dosing should not exceed 48 hours. Monitoring of plasma concentrations is not required in this instance.

Monitoring should start if therapy becomes directed, and should occur with the first dose if treatment is to continue beyond 48 hours.

Dosing relies on the Ideal Body Weight (IBW) of the patient, as well as renal function (creatinine clearance) and the type of infection present.

**If Ideal Body Weight is greater than the patient’s actual body weight, use ACTUAL body weight**
STEP ONE: Calculate Ideal Body Weight

Ideal body weights for dosing aminoglycosides.

<table>
<thead>
<tr>
<th>cm</th>
<th>Feet and inches</th>
<th>Ideal body weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>female</td>
</tr>
<tr>
<td>155</td>
<td>5’1”</td>
<td>48</td>
</tr>
<tr>
<td>160</td>
<td>5’3”</td>
<td>53</td>
</tr>
<tr>
<td>165</td>
<td>5’5”</td>
<td>57</td>
</tr>
<tr>
<td>170</td>
<td>5’7”</td>
<td>62</td>
</tr>
<tr>
<td>175</td>
<td>5’9”</td>
<td>66</td>
</tr>
<tr>
<td>180</td>
<td>5’11”</td>
<td>71</td>
</tr>
<tr>
<td>185</td>
<td>6’1”</td>
<td>75</td>
</tr>
<tr>
<td>190</td>
<td>6’3”</td>
<td>80</td>
</tr>
<tr>
<td>195</td>
<td>6’5”</td>
<td>84</td>
</tr>
<tr>
<td>200</td>
<td>6’7”</td>
<td>89</td>
</tr>
<tr>
<td>205</td>
<td>6’9”</td>
<td>93</td>
</tr>
<tr>
<td>210</td>
<td>6’11”</td>
<td>98</td>
</tr>
</tbody>
</table>

Ideal weight for male: 50kg + 0.9kg/each cm over 152cm
Ideal weight for female: 45.5kg + 0.9kg/each cm over 152cm

STEP TWO: Select appropriate dose and dosing regimen for patient

Ensure previous doses have not been administered within the last 24 hours that have been prescribed on the “STAT” order chart or on the Emergency Department Chart.

The dosing interval for empirical dosing is based on the patient’s renal function. Creatinine clearance (CrCl) can be approximated in adults using the modified Cockcroft-Gault formula (http://etg.hcn.com.au/desktop/index.htm?acc=36265). Note: eGFR obtained from BOSSnet is not the same as creatinine clearance.

*Use the most recent serum creatinine value (in the last 12-24 hours) for calculation of Creatinine Clearance.

<table>
<thead>
<tr>
<th>Creatinine clearance (mL/min)</th>
<th>Gentamicin Dose</th>
<th>Dosing interval</th>
<th>Maximum number of empirical doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe sepsis or septic shock</td>
<td>7mg/kg*</td>
<td>ONE dose only. Subsequent dose and interval based on renal function. See below</td>
<td></td>
</tr>
<tr>
<td>greater than 60 mL/min</td>
<td>4-5mg/kg</td>
<td>24 hours</td>
<td>3 (at 0, 24 and 48 hours)</td>
</tr>
<tr>
<td>40 to 60 mL/min</td>
<td>4-5mg/kg</td>
<td>36 hours</td>
<td>2 (at 0 and 36 hours)</td>
</tr>
<tr>
<td>Less than 40 mL/min</td>
<td>4mg/kg</td>
<td>Reconsider need. Give initial dose once, then seek expert advice</td>
<td></td>
</tr>
<tr>
<td>Streptococcal and Enterococcal endocarditis</td>
<td>1 mg/kg* 8 hourly</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

* Patients with severe sepsis have higher volumes of distribution and effective eGFR and therefore require a higher mg/kg dose.

Gentamicin blood levels are not required unless therapy extends beyond 48 hours.
General Administration Information

- **Infusion preparation:**
  The required dose of gentamicin is added to a 100mL minibag of sodium chloride 0.9%, OR added to 100mL of sodium chloride 0.9% in a burette.
  Total volume = 100mL + volume of gentamicin added.
  Sodium chloride 0.9% can be substituted for different compatible IV fluid as requested by the Medical Officer.

- **Volume to be removed from IV bag:** Nil.

- **Infusion Rate:** Total volume to be run over 30 minutes. Administer via infusion pump as timing critical for accurate gentamicin level interpretation.

- **Infusion pump:** Alaris LVP with Guardrails

- **Routes of administration:**
  - **IV injection:** Rarely, in severe fluid restriction. Seek expert advice.
  - **IV intermittent infusion (30 minutes):** Yes, preferred method.
  - **IV continuous infusion:** No.
  - **IM injection:** Can be given, but restricted by volume required. Not recommended. Seek Pharmacy advice.
  - **Subcut injection:** No.

- **Compatible/incompatible IV drugs/fluids:**
  See “Interactions” for information on penicillins/cephalosporins.
  Consult the Australian Injectable Drugs Handbook (‘Yellow book’) in your ward area. Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.

---

MONITORING (INCLUDING BLOOD TESTS)

Monitoring is required for all patients receiving directed or ongoing therapy exceeding 48 hours (see Indications) to ensure adequacy of dosing, delay the onset of nephrotoxicity and reduce the risk of ototoxicity. The ward pharmacist and ID/AMS Team should be contacted if extended therapy beyond 48 hours with gentamicin is being used.

Plasma levels must be taken as soon as it is decided to extend therapy beyond 48 hours (in some instances after the first dose), after each change in dose and then at least two to three times per week.

**Monitoring with extended dosing interval**

- Gentamicin level should be obtained 6 to 14 hours after the infusion is given
- Pharmacy will calculate the appropriate dose however they require:
  - Patient name / UR / DOB
  - Height and weight
  - Latest serum creatinine
  - Dose and time of last infusion
  - Duration of infusion (usually 30 minutes)

**Monitoring for endocarditis**

- Dosing of gentamicin is 1mg/kg 8 hourly
- Gentamicin level should be obtained 15 minutes prior to administration (after 24 hours of commencement or dose change)
- Target trough level is 0.5 – 1mg/L
- If trough level is greater than 1mg/L then decrease dosing interval to 12 hourly before adjusting the dose down

Pharmacy will provide dosing recommendations verbally and provide a report for patient records.

---

**UNCONTROLLED COPY IF PRINTED**

Page: 4 of 8

See BHS Intranet for current version
NURSING PRACTICE POINTS

Ensure previous doses have not been administered within the last 24 hours that have been prescribed on the “STAT” order chart, the Emergency Department chart or in the Operating Theatre as prophylaxis.

- Nephrotoxicity – report any significant decrease in urine output.
- Ototoxicity – see Precautions and Adverse Effects; report any signs or symptoms occurring in patient.
- Patient needs to be well hydrated.
- **Pathology request forms for gentamicin levels** – require the following information added
  - the frequency of administration
  - time of administration of the previous dose and the previous dose
  - time blood drawn
  - “For streptococcal or enterococcal endocarditis” (if applicable)
- **Review and confirmation by Medical Officer** - Once a gentamicin level (excluding 8 hourly trough levels) has been taken, no more doses are to be given until the results have been reviewed and next dose confirmed by a Medical Officer.

ADVERSE EFFECTS

Vestibular and auditory ototoxicity

Vestibular toxicity may be irreversible; it can occur even when drug concentrations are within the normal therapeutic range and may become apparent early in the course of treatment or weeks after therapy has ceased. Patients should be clinically monitored and advised that hearing and balance problems can occur, and asked to report any hearing or balance problems immediately.

Baseline audiometry should be recorded close to the time of initiation of therapy and repeated periodically if the course of aminoglycoside extends beyond 14 days. This should be repeated periodically during treatment if there are concerns and at the end of treatment.

They should be asked regularly if they have the following symptoms:

- trouble reading the paper
- ataxia
- dysequilibrium and loss of balance
- oscillopsia (the subjective sensation that the field of vision jumps up and down)
- loss of visual acuity during head movement.

Gentamicin must be ceased if any new hearing or balance impairment is noted, ototoxicity may be irreversible

Nephrotoxicity

Nephrotoxicity is usually a reversible adverse effect and can be anticipated if treatment lasts longer than 7-10 days. Generally presents as gradually worsening non-oliguric renal failure with increasing serum creatinine and proteinuria, but may present as tubular necrosis.

Rare reactions

- Anaphylaxis, bronchospasm, neuromuscular blockade (see Precautions), oliguria, peripheral neuropathy.

---

**DRUG PRESENTATIONS, LOCATION AND STORAGE**

Gentamicin 80 mg/2 mL ampoules.

Imprest locations (at the time of guideline development): 5N, 4N, 4S, 3N, 3S, 2S, 2N, CCU, ED, Theatre, CVS, Endoscopy, SSU, Dialysis, IRP, JGU, Gandarra.

Store at room temperature. Protect ampoules from light and avoid freezing.

---

**RELATED DOCUMENTS**

SOP0001 Clinical Care
POL0083 Antibiotic Policy
CPP0262 Antimicrobial Stewardship

---

**REFERENCES**

APPENDIX 1

Calculation of creatinine clearance (CrCl)


Use ideal weight if actual weight 20% greater than ideal weight.

Alternatively, CrCl can be calculated manually using the Cockcroft-Gault formula below, and ideal body weight from the print version of the Therapeutic Guidelines - Antibiotic, Version 15, 2014 using Table 32 (page 609) or the manual equations from Table 1 below.

Males
\[
CrCl = \frac{(140 - \text{Age (yr)}) \times \text{weight (ideal kg)}}{0.814 \times \text{serum creatinine (micromol/L)}}
\]

Females
\[
CrCl = \frac{(140 - \text{Age (yr)}) \times \text{weight (ideal kg)} \times 0.85}{0.814 \times \text{serum creatinine (micromol/L)}}
\]

The calculation of creatinine clearance in these methods is only applicable if renal function is stable, and may overestimate CrCl in patients of low muscle mass.

APPENDIX 2

DRUG INTERACTIONS

- **Nephrotoxic drugs** (e.g. vancomycin, cisplatin, amphotericin, cephalosporins, colistimethate, frusemide, bumetanide, ethacrynic acid, mannitol, nonsteroidal anti-inflammatory, cyclosporin, polygeline, tacrolimus, lymph,cidofovir, capreomycin, possibly clindamycin) - can increase nephrotoxic adverse reactions from gentamicin. Gentamicin levels and serum creatinine may require more frequent monitoring to ensure accumulation is not occurring.

- **Ototoxic drugs** (e.g. frusemide, bumetanide, ethacrynic acid, cisplatin, carboplatin, capreomycin) - can increase ototoxic adverse reactions from gentamicin. Gentamicin levels and serum creatinine may require more frequent monitoring to ensure accumulation is not occurring.

- **Suxamethonium and non-depolarising neuromuscular blockers** (atracurium, cisatracurium, mivacurium, pancuronium, rocuronium and vecuronium) – gentamicin can prolong effects of these drugs and may lead to respiratory insufficiency; reduce neuromuscular blocker dose and monitor neuromuscular blockade closely.

- **Magnesium sulfate (parenteral), capreomycin, botulinum toxin** - additive neuromuscular blockade when used with gentamicin; use combination cautiously, monitor respiratory function.

- **Intravenous azoles** (fluconazole, voriconazole) - gentamicin serum levels may be reduced requiring a higher dose than expected. Similarly gentamicin dose may need reducing if intravenous azole therapy is ceased.

- **Intravesicular BCG treatment** - all antibiotics (including gentamicin) can decrease the effectiveness of BCG and co-administration should be avoided.

- **Bisphosphonates** (alendronate, clodronate, etidronate, disodium pamidronate, ibandronic acid, risedronate, tiludronate, zoledronic acid) – some reports of hypocalcaemia with gentamicin, monitor where appropriate.

- **Algalsidase (alpha and beta)** - gentamicin may reduce the effect of agalsidase, avoid giving concomitantly.

- **Tenofovir** - may decrease the clearance of gentamicin leading to toxicity.
APPENDIX 3: GENTAMICIN DOSING AND MONITORING SUMMARY

Gentamicin is dosed using IDEAL body weight
Use actual body weight if less than patient’s ideal body weight

***Ensure previous doses have not been administered within the last 24 hours that have been prescribed on the “STAT” order chart, the Emergency Department chart or in the Operating Theatre***

Therapeutic drug monitoring should be considered after the first dose if treatment is likely to extend beyond 48 hours

- **Patients WITH signs of sepsis**
  - 7mg/kg for single dose then review

- **Empiric treatment without signs of sepsis**
  - 4-5mg/kg for single dose then review (Use 4mg/kg dose if CrCl less than 40)

**Subsequent dosing interval dependent upon renal function**

- **CrCl less than 40mL/min**
  - Reconsider need. Give initial dose once, then seek expert advice
  - Maximum number of doses before levels required: **ONE**

- **CrCl 40-60mL/min**
  - Frequency: every 36 hours
  - Maximum number of doses before levels required: **TWO**

- **CrCl greater than 60mL/min**
  - Frequency: every 24 hours
  - Maximum number of doses before levels required: **THREE**

**IF DIRECTED THERAPY IS CONTINUING**

**Discuss with Pharmacy**

- **Directed therapy**: Level is to be taken **6 to 14 hours** after the infusion is given. Pharmacy will calculate the ongoing dose
  - **Endocarditis synergy**: Trough level to be taken 15 minutes prior to dose. Aim: 0.5 – 1mg/L

For additional information, including detailed requirements for therapeutic drug monitoring, see Gentamicin (sulfate) Drug Guideline DRG0006