

Intravenous Gentamicin use in Adult (5mg/kg)

Background

This policy covers the use of intravenous (IV) gentamicin in adults using a dose of 5mg/kg. This dosing guidance was developed by Greater Glasgow and Clyde (GGC) based on local research and the published evidence below.

The policy is for the use of gentamicin for the treatment of infection only. SAPG recommendations on gentamicin dosing for surgical prophylaxis are provided elsewhere.

The guidance **does not apply** to gentamicin use in the following:

- synergistic treatment of endocarditis or *Staphylococcal* bone infection
- patients treated in Renal units or receiving haemodialysis or haemofiltration
- major burns
- ascites
- age < 16 years
- cystic fibrosis (refer to local guidelines), and
- pregnancy (refer to local guidelines).

Contra-indications and cautions

- Contra-indications to gentamicin therapy – hypersensitivity, myasthenia gravis.
- Cautions to gentamicin therapy:
 - Patients with decompensated liver disease - aminoglycosides are associated with an increased risk of renal failure.
 - Concurrent administration of neurotoxic and / or nephrotoxic agents increases the risk of gentamicin toxicity. Review therapy and consider amending or withholding nephrotoxic drugs during gentamicin treatment. Avoid co-administration with the following:
 - neuromuscular blockers
 - other potentially nephrotoxic (e.g. NSAIDs and ACE Inhibitors) or ototoxic drugs
 - potent diuretics, and
 - other aminoglycosides.
 - This list is not exhaustive – consult www.medicines.org.uk for a full list.
 - Chronic Kidney Disease (CKD) Stage 4 or more, known or suspected acute kidney injury in the previous 48 hours ($\geq 50\%$ increase in baseline serum creatinine or oliguria > 6 hours). If gentamicin is clinically indicated, give one dose as per guidance and check with microbiology or an infection specialist before giving a second dose.

Prescribing and documentation

- To improve the prescribing of gentamicin, ensure consistency and reduce risk, standardised charts (agreed nationally) should be used to document the prescription, administration and monitoring of gentamicin. These should be used for prescribing treatment doses of gentamicin in conjunction with the existing inpatient prescription and administration record and the medical / nursing documentation.
- These charts contain a step-wise approach to safe and effective prescribing and key points of advice on monitoring, interpreting and re-prescribing.

- An Antimicrobial app and/or an online calculator is available in all boards and should be used to calculate the initial dose.

Reference: Anaizi et al. Once-daily dosing of aminoglycosides. A consensus document. *International J Clin Pharmacol Ther* 1997; 35: 223 – 226

STEP 1: Calculate, prescribe and administer the first dose

- To reduce risk of mortality, commence gentamicin administration within 1 hour of recognising sepsis.
- If creatinine is known – use the online calculator or app (preferred method). The guidelines in Table 1 (below) can be used if the online calculator is not available. The dose amount and dosage interval are based on estimated creatinine clearance (Box 1) and **actual** body weight.
- If creatinine is not known – use an initial dose of 5 mg/kg gentamicin (maximum 400 mg) or, if chronic kidney disease (CKD) 5, use 2.5 mg/kg (maximum 180 mg) on advice of senior staff. Calculate the dose using **actual** body weight.
- Give the recommended dose by infusion in 100 mL sodium chloride 0.9% over 30 minutes and ensure the time of administration is noted on the medicine chart.

Box 1: Estimation of creatinine clearance (CrCl)

The following ‘Cockcroft Gault’ equation can be used to estimate creatinine clearance (CrCl)

$$\text{CrCl} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)} \times 1.23 \text{ (male) OR } 1.04 \text{ (female)}}{\text{(mL/min)} \quad \text{serum creatinine (micromol/L)}}$$

Cautions:

- Use actual body weight or maximum body weight whichever is lower.
See <https://www.sapg.scot/media/4471/maximum-body-weight-table.pdf>
- In patients with low creatinine (< 60 micromol/L), use 60 micromol/L.
- Note: Use of estimated glomerular filtration rate (eGFR) is not recommended.

Table 1: Initial GENTAMICIN doses and dose intervals

Actual body weight → Creat Cl (mL/min) ↓	40 - 49 kg	50 - 59 kg	60 - 69 kg	70 - 80 kg	> 80 kg
< 21	2.5 mg/kg (max 180 mg) then take a sample after 24 hours				
21 - 30	180 mg 48 hourly	200 mg 48 hourly	240 mg 48 hourly	240 mg 48 hourly	260 mg 48 hourly
31 - 40	200 mg 48 hourly	240 mg 48 hourly	280 mg 48 hourly	300 mg 48 hourly	320 mg 48 hourly
41 - 50	240 mg 48 hourly	280 mg 48 hourly	320 mg 48 hourly	360 mg 48 hourly	400 mg 48 hourly
51 - 60	200 mg 24 hourly	240 mg 24 hourly	280 mg 24 hourly	300 mg 24 hourly	320 mg 24 hourly
> 60	240 mg 24 hourly	280 mg 24 hourly	320 mg 24 hourly	360 mg 24 hourly	400 mg 24 hourly

Caution: If the patient weighs < 40 kg and CrCl is ≥ 21 mL/min, give a single dose of 5 mg/kg then take a sample 6 – 14 hours after the dose and follow the instructions in Step 2.

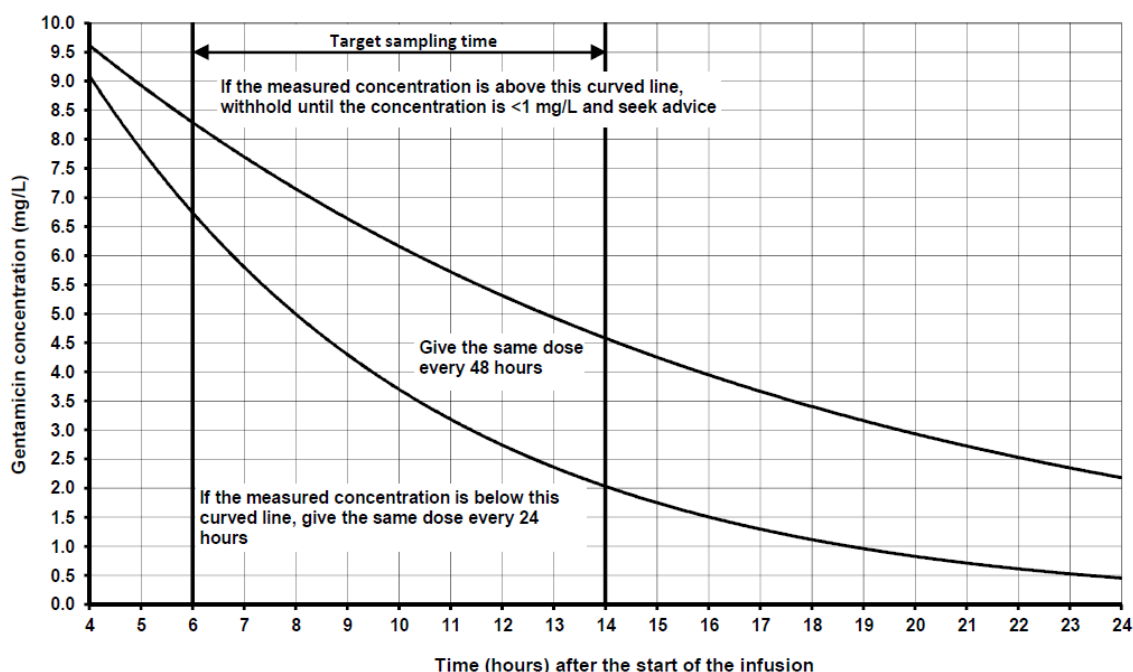
Note that patients who have unusual clinical characteristics, such as weight < 40 kg, weight >120 kg, age >90 years may require dose adjustments and require close monitoring. Contact pharmacy for advice.

STEP 2: Monitor creatinine and gentamicin concentrations and reassess the dosage regimen

Concentrations are meaningless unless the dose & sample times are recorded accurately

If creatinine clearance is ≥ 21 mL/min

- Take a blood sample 6-14 hours after the start of the first gentamicin infusion.
- Record the exact time of all gentamicin samples on the gentamicin prescribing chart AND on the sample request form.
- Record the serum concentration on the gentamicin prescribing chart.
- Plot the concentration measurement on the graph and reassess the dose / dosing interval as indicated.
- This will indicate one of three options:
 - 1) continue the present dosage regimen
 - 2) adjust the dosage interval
 - 3) withhold and resample after 24 hours



If creatinine clearance is < 21 mL/min

- Take a blood sample 24 hours after the start of the first gentamicin infusion.
- Record the exact time of all gentamicin samples using the gentamicin prescribing chart AND on the sample request form.
- If therapy is to continue, take additional blood samples at least every 24 hours and give a further dose once the measured concentration is < 1 mg/L.

General points

- Document the action taken in the medical notes and on the gentamicin prescribing chart.
- Undertake pre-prescribing checks (Boxes 2 and 3) to assess the risk of renal toxicity and ototoxicity.
- Prescribe the next dose as appropriate.
- Seek advice from pharmacy or microbiology if you are unsure how to interpret the result or if the concentration is lower than expected.

- Doses up to 600 mg may be required in obese patients but seek advice before giving doses > 400mg.
- If a blood sample is not taken, is lost or is taken at wrong time *and* if there is any concern about the patient's renal function, take a sample 20-24 hours after the start of the gentamicin infusion and wait for the result before giving the next dose. Otherwise, take a blood sample after the next dose.

If the measured concentration is unexpectedly HIGH or LOW, consider the following:

- Were dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Was the sample taken during drug administration?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?

If in doubt, take another sample before re-prescribing and / or contact pharmacy for advice

STEP 3: Assess daily the ongoing need for gentamicin and signs of toxicity

- Take a further blood sample 6-14 hours after the dose, at least every 2 days.
- If the gentamicin concentration is unexpectedly high or if renal function alters, daily sampling may be necessary.
- To minimise the risk of toxicity, duration of treatment should normally be limited to 72 hours. All gentamicin prescriptions that continue beyond 3-4 days of treatment must be discussed with microbiology or an infection specialist. Consider changing to an oral alternative - refer to the IV to Oral switch policy.

Box 2: Renal toxicity

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| <ul style="list-style-type: none"> ▪ Monitor creatinine daily. Seek advice if renal function unstable (change in creatinine level). ▪ Signs of renal toxicity include increase in creatinine or decrease in urine output/oliguria. ▪ Consider an alternative agent if creatinine is rising or the patient becomes oliguric. |
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Box 3: Ototoxicity

- Ototoxicity secondary to gentamicin is independent of drug concentration. It is suggested by any of the following: new tinnitus, dizziness, poor balance, hearing loss or oscillating vision.
- Toxicity is associated with prolonged aminoglycoside use (usually > 10 days but may be > 72 hours) and is secondary to drug accumulation within the inner ear. Multiple courses of gentamicin are also a risk factor for ototoxicity.
- Stop treatment if ototoxicity is suspected and refer to microbiology or an infection specialist for advice on future therapy and refer to ENT for assessment.
- If gentamicin continues for > 7 days, consider referring to audiology for assessment.