Once Daily Gentamicin: Administration and Monitoring in Adults

(excludes patients receiving renal replacement therapy)

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Gloucestershire Hospitals NHS Foundation Trust

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Objective:
Policy for the administration and monitoring of once-daily gentamicin at Gloucestershire Hospitals NHS Foundation Trust (GHNHSFT).

Background/policy statement:
Gentamicin is the aminoglycoside of choice at GHNHSFT due to its lower cost and suitability for most infections requiring treatment with an aminoglycoside. Tobramycin and amikacin are normally reserved for treatment of infections that require treatment with an aminoglycoside antibiotic where the causative organism is resistant to gentamicin, or on the advice of a Consultant Microbiologist, or specialist physician (eg Respiratory Consultant). Tobramycin is the preferred aminoglycoside for treatment of respiratory tract *Pseudomonas* species infections.

Aminoglycoside antibiotics such as gentamicin must be administered parenterally as they are poorly absorbed from the GI tract. In general, once-daily administration is now recommended in most clinical situations. Once daily gentamicin is:

- As effective as multiple dosing regimes
- Less toxic (less nephrotoxicity & ototoxicity)
- More convenient to administer and monitor
- More economical

Wherever possible, parenteral therapy should not exceed 7 days.

The policy is for the use of gentamicin for the treatment of infection only. Guidance on gentamicin dosing and use for surgical prophylaxis can be found in individual surgical prophylaxis guidelines on the GHNHSFT Intranet Antimicrobial Resources pages.

Cautions and contraindications:
The once daily guidance **does not apply** to gentamicin use in the following:

- synergistic treatment of endocarditis (where some treatment regimens use twice daily or thrice daily dosing) or *Staphylococcal* bone infection
- patients treated in Renal units or receiving haemodialysis or haemofiltration – (see The Renal Handbook for dosage information in renal replacement therapies or contact nephrologist).
- major burns (>20% total body surface area)
- ascites
- age < 16 years
- cystic fibrosis (where higher doses of aminoglycosides are normally required)

Contra-indications

- Myeloma patients
- Myasthenia gravis
- Patients allergic (hypersensitive) to gentamicin

Cautions:

- **Chronic Kidney Disease (CKD) Stage G4 or more**, known or suspected acute kidney injury (AKI) in the previous 48 hours (50% increase in baseline serum creatinine or oliguria > 6 hours). If gentamicin is clinically indicated, give one dose as per guidance and check with ward pharmacist or nephrologist before giving a second dose. Gentamicin should be used with caution in patients with **renal impairment**. See page 6 for dosage recommendations in renal impairment

- **Auditory or vestibular dysfunction** - Ototoxicity secondary to gentamicin is independent of drug concentration. Likely signs and symptoms may include: 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.
  There have also been observed cases of an increased risk of ototoxicity with aminoglycosides administered to patients with mitochondrial mutations, particularly the m.1555A>G mutation, including cases where the patient's aminoglycoside serum levels were within the recommended range. Some cases were associated with a maternal history of deafness and/or mitochondrial mutation. Mitochondrial mutations are rare, and the penetrance of this observed effect is unknown.
  Stop treatment if ototoxicity is suspected and refer to microbiologist or antimicrobial pharmacist for advice on alternative therapy. If gentamicin continues for >7 days, consider referring to Audiology for assessment. 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 where possible:
  - neuromuscular blockers
  - other potentially nephrotoxic (e.g. NSAIDs and ACE Inhibitors) or ototoxic drugs
  - potent diuretics
  - other aminoglycosides

  This list is not exhaustive – consult the Summary of Product Characteristics (eSPC) for a full list (www.medicines.org.uk)

- **Conditions characterised by muscular weakness** (aminoglycosides may impair neuromuscular transmission)

- **Dehydration** should be corrected before starting an aminoglycoside

Dosage:

The dose will be dependent on:

- weight (ideal body weight or Adjusted/Obese dose body weight)* - see below
- age
- renal function – see appendix 1 for calculating Creatinine clearance (CrCl calculator)
- For maternity sepsis, use pregnancy booking weight to calculate the dosage

	CrCl above 30ml/min	CrCl of 10-30ml/min	CrCl less than 10ml/min
Age 65 and over	3mg/kg* iv od	2mg/kg* iv od	**Do not give gentamicin**
Age under 65 years	5mg/kg* iv od	3mg/kg* iv od	**Do not give gentamicin**

*Use ideal body weight (IBW) rather than actual body weight (ABW) because gentamicin distributes poorly in fat.

To calculate **ideal body weight**, use the following equation or see appendix 2:

Ideal body weight (Male) = 50kg + (2.3kg x height in inches over 5 feet)
Ideal body weight (Female) = 45.5kg + (2.3kg x height in inches over 5 feet)

For obese patients (BMI>30 or 120% of ideal body weight) it is recommended that the dose is calculated using the patient's adjusted/obese dose body weight.

To calculate **adjusted/obese body weight**, use the following equation or use the Ideal Body Weight and Adjusted/Obese Body Weight calculator (appendix 2) **(NOTE: Do not use calculator if patient is under 5ft or 152.5cm in height.**

Obese/adjusted dosing body weight (ODBW/ADBW) = IBW + 0.4 (ABW - IBW)

Round dose up or down to the nearest 20mg

Minimum doses – If after dose re-calculation the revised dose is less than 2mg/kg, strongly consider alternative gram negative cover. See Antibiotic Guidelines for advice on choices, and review recent /current Microbiology results, including culture and sensitivity results for Gram negative organisms.

Maximum doses – if a dose is calculated as being greater than 500mg, check that the dose has been calculated correctly based on ideal body weight or obese dosing body weight, depending on whichever of these is applicable.

The dose can be given as an intravenous infusion in 100mls of dextrose 5% or sodium chloride 0.9% over 60 minutes.

When to give the dose

The first dose of gentamicin may be given at any time of day (i.e. as soon as the first dose is needed).

Subsequent doses should be moved to a time that is convenient for both the patient (i.e. not overnight) and the Chemical Pathology Department for the purposes of monitoring gentamicin levels

(i.e. no samples for gentamicin levels should be sent for testing between 11pm and 6am).

Evening dosing is preferred. To facilitate this, the second dose may be given 18 to 36 hours after the first dose provided that the first gentamicin level is within the recommended range (see monitoring/interpretation below) and the patient's renal function has not changed significantly

Monitoring:

A post-dose level is required. A single serum sample should be obtained 12 to 18 hours after the dose and sent to CHEMICAL PATHOLOGY. As there is flexibility about the timing of the sampling, a time which is convenient for the patient and the laboratory should be chosen.
Preferably, samples should not be collected or sent for testing between 11pm and 6am.
Electronic blood sample request forms must include the following information:

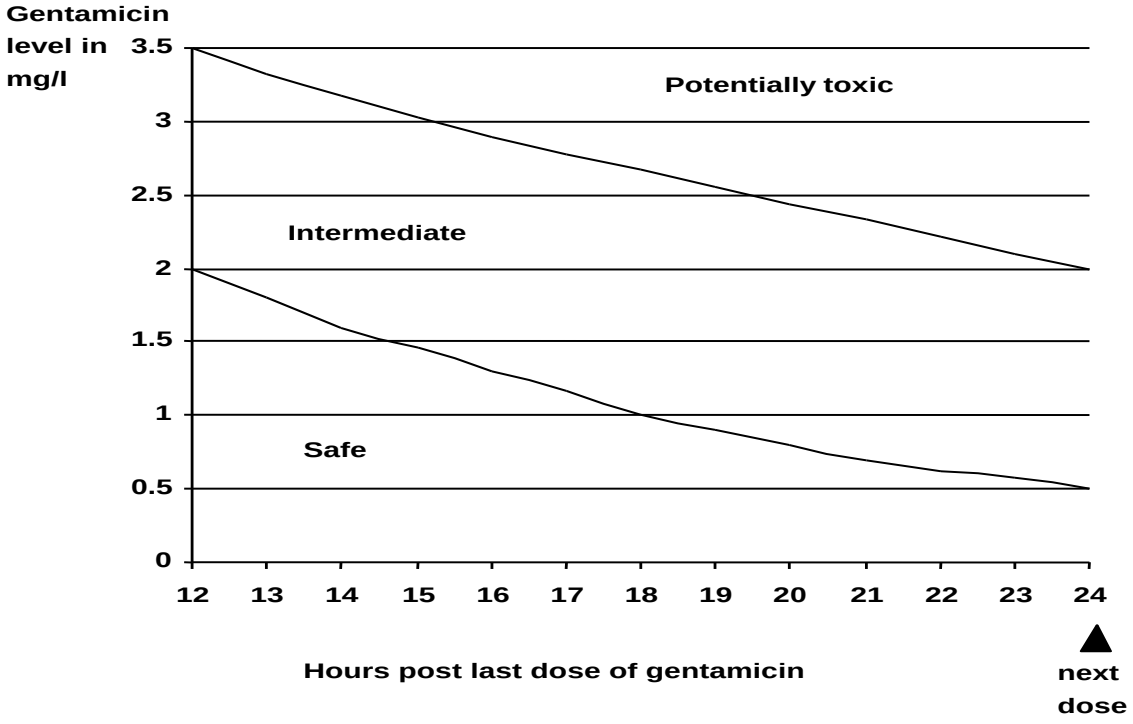
- Date and time of last dose
- Date and time of blood sample taken
- Dose or dose per kg used (e.g. 5mg/kg)
- Dosing regimen (e.g. once daily dosing)

Target serum concentration for once-daily gentamicin:

12 hours post dose = <2mg/L
18 hours post dose = <1mg/L

Interpretation:

Take gentamicin level 12-18 hours after the first dose. Plot the result of the gentamicin level on the graph below to decide if the level is safe (recommended range), intermediate or potentially toxic.



Safe: If the serum gentamicin level is ≤ 2mg/l after 12 hours and ≤1mg/l after 18 hours it is safe to give the next dose on time (same dose).

Intermediate: If the level falls in the intermediate area a dose reduction needs to be made, this reduced dose can be given when the next dose is due. If after dose re-calculation the revised dose is less than 2mg/kg, strongly consider alternative Gram negative cover. Consult empirical Antibiotic Guidelines for information and review recent/current Microbiology results..

Dose reduction to a new dose will be required as per this equation:

$$\textit{New Dose} = \frac{\text{Previous daily dose x Target serum value}}{\text{Actual serum level}}$$

The **Target Serum Value** is the intersection of time (hours post last dose of gentamicin) and the line separating the Intermediate and Safe areas on the graph above.

Serum gentamicin levels should be rechecked 12 to 18 hours after the new revised dose has been administered.

Example: Patient has a level of 2.5mg/L at 16 hours post dose

$$\text{New dose} = \frac{360\text{mg} \times 1.3}{2.5} = 187\text{mg rounded to } 180\text{mg}$$

Potentially toxic: Omit the next dose if the level is in the potentially toxic area. Consider whether it is safe to continue ongoing gentamicin during the current treatment episode or whether alternative antibiotic treatment (specifically for Gram negative cover) is required. Discuss with Microbiology if necessary. Generally it is recommended to stop gentamicin in patients whose levels are genuinely potentially toxic..

If gentamicin levels are within the recommended range with normal renal function then monitor levels and U&Es twice weekly.

Caution must be used when using this graph to interpret levels taken from patients with renal dysfunction, as their concentration-time-curve may be different.

Appendix 1

Calculating renal function

Cockroft-Gault equation for estimating creatinine clearance:

Creatinine Clearance (GFR) = $\frac{(140 - \text{Age}) \times \text{Weight (Kg)} \times F}{\text{Serum Creatinine (µmol/litre)}}$

Where F = 1.23 (For Men)
1.04 (For Women)

Online calculator (CrCl calculator)

Appendix 2

Calculating ideal body weight and obese/adjusted body weight

Ideal Body Weight and Adjusted Body Weight calculator
(NOTE: Do not use calculator if patient is under 5ft or 152.5cm in height.

Alternatively, obtain the ideal body weight from the table below and use the following equation to calculate an obese dosing body weight:

Adjsuted/Obese dosing body weight = IBW + 0.4 (ABW - IBW)

Males

Height (ft'in)	Height (cm)	IBW (kg)
4'10	147	45.4
4'11	150	47.7
5'0	152.5	50.0
5'1	155	52.3
5'2	157.5	55.6
5'3	160	57.0
5'4	162.5	59.2
5'5	165	61.5
5'6	167.5	63.8
5'7	170	66.1
5'8	172.5	68.4
5'9	175	70.7
5'10	177.5	73.0
5'11	180	75.3
6'0	183	77.6
6'1	185.5	79.9
6'2	188	82.2
6'3	190.5	84.5
6'4	193	86.8
6'5	195.5	89.1
6'6	198.5	91.4
6'7	201	93.7

Females

Height (ft'in)	Height (cm)	IBW (kg)
4'8	142	36.3
4'9	144.5	38.6
4'10	147	40.9
4'11	150	43.2
5'0	152.5	45.5
5'1	155	47.8
5'2	157.5	50.1
5'3	160	52.4
5'4	162.5	54.7
5'5	165	57.0
5'6	167.5	59.3
5'7	170	61.6
5'8	172.5	63.9
5'9	175	66.2
5'10	177.5	68.5
5'11	180	70.8
6'0	183	73.1
6'1	185.5	75.4
6'2	188	77.7

For further advice or clarification please contact:

☎ Medicines Information:	CGH ext. 3030	GRH ext. 6108
☎ Microbiology:	CGH ext. 4430	GRH ext. 5054

Selected References:

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Consideration at authorised groups (e.g. Board, Board sub committees, Policy Group, Clinical policies Sub Group, Departmental meetings etc)

Name of Group	**Minute details**	**Date considered**
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