

GUIDANCE ON USE OF GENTAMICIN and VANCOMYCIN IN ADULTS

1. Background

Gentamicin and vancomycin are increasingly being used in hospitals for both surgical prophylaxis and treatment of infections. Determination of appropriate doses for individual patients frequently presents problems for junior medical staff due to the complexity of the calculations involved and confusion between BNF guidance and local policies. In addition, each NHS Board has its own policy therefore staff moving between Boards do not become familiar with a single approach.

Documentation of dose and sample times is often poor and serum concentration monitoring is often performed incorrectly leading to misinterpretation of results and inappropriate dosage adjustment. The use of gentamicin and vancomycin therefore presents a significant risk both to patient safety and also to NHS Board Clinical Governance.

To address these problems, the Scottish Antimicrobial Prescribing Group (SAPG) has consulted with NHS Board Antimicrobial Management Teams (AMTs) to develop a consensus view on standardisation of policies for gentamicin and vancomycin. In addition SAPG has collaborated with NHS Education Scotland to provide additional training on gentamicin and vancomycin for junior doctors within the Doctors On-line Training System (DOTS) mandatory training on use of antimicrobials.

2. Scope

The gentamicin regimens are for the treatment of infections only whereas the vancomycin regimen is for treatment and prophylaxis.

Gentamicin dosing for surgical prophylaxis varies depending on the health board and SAPG recommendations are provided elsewhere¹.

This guidance also does not apply to use of gentamicin for synergistic treatment of infections or use of vancomycin and gentamicin in Renal Unit patients or those on haemofiltration.

3. Dose calculation

- An easily accessible on-line calculator for creatinine clearance or drug dosage calculation² should be made available on all NHS Board intranet sites. Calculators are available to download from the SAPG website.
- AMTs need to heighten awareness that an on-line calculator is available and should be used in preference to manual calculation of the dosage regimen using the Cockcroft-Gault equation for creatinine clearance.
- In patients with low creatinine (< 60 micromol/L), 60 micromol/L should be used in the on-line calculator or the equation to avoid over estimating creatinine clearance.

4. Body weight calculation

- Patient weight and height are required to calculate gentamicin and vancomycin dosage regimens
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- Use actual body weight up to a maximum value calculated from Ideal body weight (IBW) plus 20% to calculate creatinine clearance when using the Cockcroft-Gault equation.
- IBW can be calculated as follows:
Males 50.0 kg, Females 45.5 kg + 2.3 kg per inch above 5 feet (or 2.5 cm above 152 cm). Alternatively a table of IBW (Appendix 4) can be used.
- A table of IBW + 20% (maximum body weight, MBW) is presented in Appendix 5.
- Vancomycin loading dose should be based on actual body weight (ABW).
- The subsequent vancomycin dosage regimen is based on estimated creatinine clearance.
- For the initial gentamicin dose amount, the NHS Greater Glasgow & Clyde policy/on-line calculator uses ABW and estimated creatinine clearance.
- For the initial gentamicin dose amount, the Hartford policy uses ABW. If the patient weighs >20% above IBW, a corrected dosing weight is used
$$\text{Dosing weight} = \text{IBW} + 0.4 (\text{ABW} - \text{IBW}).$$
- To prevent overdosing severely obese patients, both vancomycin and gentamicin doses should be capped at a maximum dose.

5. Vancomycin regimen – for treatment and prophylaxis of infections

- National consensus supports adopting the new NHS Greater Glasgow & Clyde vancomycin policy³, which involves all patients receiving a loading dose based on actual body weight followed by intermittent infusions based on creatinine clearance. This policy follows recommendations from the recent Vancomycin Therapeutic Guidelines publication by the Infectious Diseases Society of America⁴.
- For Intensive Care patients, an alternative continuous infusion regimen is preferred.

See Appendix 1 for details of the recommended policy.

6. Gentamicin regimens – for treatment of infections only

Dosage

- Two policies for 'extended interval' gentamicin are widely used in Scotland. National consensus is that moving to one policy is not acceptable at this time due to lack of evidence that one policy is better/safer than the other.

- Boards should follow one of these policies - either the new Greater Glasgow & Clyde policy^{5,6} or the Hartford⁷ 7mg/kg policy. Details of both policies are discussed within the DOTS programme.
- Exclusions to once daily regimens – synergistic treatment of endocarditis and *Staphylococcal* bone infection, pregnancy, major burns, ascites, age < 16 years, patients on dialysis.
- Cautions - Chronic Kidney Disease CKD Stage 4 or more, known or suspected acute kidney injury in previous 48 hours ($\geq 50\%$ increase in baseline serum creatinine or oliguria > 6 hours). If gentamicin is clinically indicated, give one dose and check with Microbiology or an ID Consultant before giving a second dose.
- Duration of treatment with gentamicin should be limited to minimise toxicity. All prescriptions should be reviewed after 72 hours in conjunction with microbiology results and treatment continued only on the advice of a Microbiologist or ID Consultant.
- Vestibular and oto-toxicity secondary to gentamicin is independent of drug concentration and is suggested by any of the following: dizziness, unsteadiness on feet, tinnitus, bobbing oscillopsia (vertical bouncing of surroundings), hearing loss, nausea or vomiting. 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. Patients receiving therapy beyond 72 hours should be warned of this potential side-effect and drug should be discontinued at the earliest sign of toxicity.

Monitoring

- All samples for gentamicin monitoring should ideally be taken 6 – 14 hours after the initial dose has been given and dose adjustment determined using the appropriate nomogram.
- Monitor renal function by measuring serum creatinine three times a week or daily if unstable. An increase in creatinine indicates a need for dose adjustment and could suggest gentamicin toxicity. If serum creatinine rises by more than 30 micromol/L, the dosage regimen may need to be altered. Review therapy with a Microbiologist or ID Consultant.
- Patients may be asymptomatic but still have toxic gentamicin levels and toxicity can develop even in patients with normal gentamicin levels. The best way of avoiding toxicity is to ensure that treatment duration is no more than 3 days unless this is necessary on clinical grounds.

See Appendices 2 and 3 for examples of recommended policies.

References

1. Guidance on surgical prophylaxis
www.scottishmedicines.org.uk/smc/files/Microsoft%20Word%20-%20SAPG%20Guidance%20on%20surgical%20prophylaxis.pdf
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3. Thomson AH, Staatz, CE, Tobin C, Gall M, Lovering AM.
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4. Rybak MJ, Lomaestro BM, Rotschafer JC, Moellering RC, Craig WA, Billeter M, Dalovisio JR, Levine DP.
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Development of guidelines for gentamicin dosing.
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Proposal for changes to gentamicin dosage guidelines 2008 (unpublished).
7. Freeman CD, Nicolau PD, Belliveau PP, Nightingale CH.
Once-daily dosing of aminoglycosides: review and recommendations for clinical practice.
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Appendix 1 VANCOMYCIN POLICY

1. Loading infusion

Actual body weight	Dose	Volume of sodium chloride 0.9%	Duration of infusion
<40 kg	750 mg	250 ml	1.5 hours
40 – 59 kg	1000 mg	250 ml	2 hours
60 – 90 kg	1500 mg	500 ml	3 hours
> 90 kg	2000 mg	500 ml	4 hours

2. Maintenance intermittent infusion

- Calculate creatinine clearance using on-line calculator or Cockcroft- Gault equation and select dose required using the table below. Alternatively an on-line dose calculator can be used to calculate the initial dosage regimen.
- **DO NOT use eGFR.**
- Dilute doses up to 1250 mg in 250 ml sodium chloride 0.9% and doses between 1250 mg and 2500 mg in 500 ml sodium chloride 0.9%. Glucose 5% may be used in patients with sodium restriction.
- Give first maintenance infusion 12, 24 or 48 hours after loading infusion according to table below:

VANCOMYCIN PULSED INFUSION - INITIAL DOSAGE GUIDELINES		
CrCl (ml/min)	Dose amount	Dose Interval
< 20	500 mg over 1 hour	48 hours
20 - 29	500 mg over 1 hour	24 hours
30 - 39	750 mg over 1.5 hours	24 hours
40 - 54	500 mg over 1 hour	12 hours
55 - 74	750 mg over 1.5 hours	12 hours
75 - 89	1000 mg over 2 hours	12 hours
90 - 110	1250 mg over 2.5 hours	12 hours
>110	1500 mg over 3 hours	12 hours

N.B. For 12 hourly regimens the daily dose can be split into 3 equal doses and given 8 hourly. This approach is especially useful for patients who require unusually high doses. In the above table, 1500 mg 12 hourly could be given as 1000 mg 8 hourly and 750 mg 12 hourly could be given as 500 mg 8 hourly.

Monitoring of vancomycin concentrations

- **Concentrations are meaningless unless the dose and sample time are recorded accurately.**
- Take a trough sample at the end of the dosage interval after 24 hours for patients on a 12 hourly regimen or after 48 hours for patients on 24 or 48 hourly regimens.
- Take samples daily if the patient has unstable renal function
- Record the time of the last dose and the blood sample time on the request form and the blood sample time on the sample tube.

Target trough concentration: 10 – 20 mg/L

- If a patient is seriously ill or failing to respond to vancomycin, check the minimum inhibitory concentration (MIC) by E test, even for isolates reported as susceptible. If MIC is measured as 1 - 2 mg/L, increase the dose to achieve a target trough concentration of 15-20 mg/L or consider a change in therapy.

Adjustment of vancomycin doses

- Always check that the dosage history and sampling time are appropriate before interpreting the result
- Seek advice from pharmacy or microbiology if you need help to interpret the result.

Vancomycin concentration	Suggested dose change
<10 mg/L	Increase dose by 50% or seek advice
10 – 20 mg/L	Maintain the present dose
>20 mg/L	Stop until <20 mg/L then seek advice

Appendix 2 GENTAMICIN POLICY (GGC)

- The initial dosage regimen can be determined using an online dose calculator or use the table below.
- The dose amount and dosage interval are based on actual body weight and estimated creatinine clearance. Use maximum dosing weight (appendix 5) to estimate creatinine clearance in obese patients (actual body weight > 20% above ideal body weight).
- **Use of eGFR is not recommended**
- Give the recommended dose by infusion in 100ml sodium chloride 0.9% or glucose 5% over 30 – 60 minutes.

Table of initial GENTAMICIN doses and dose intervals

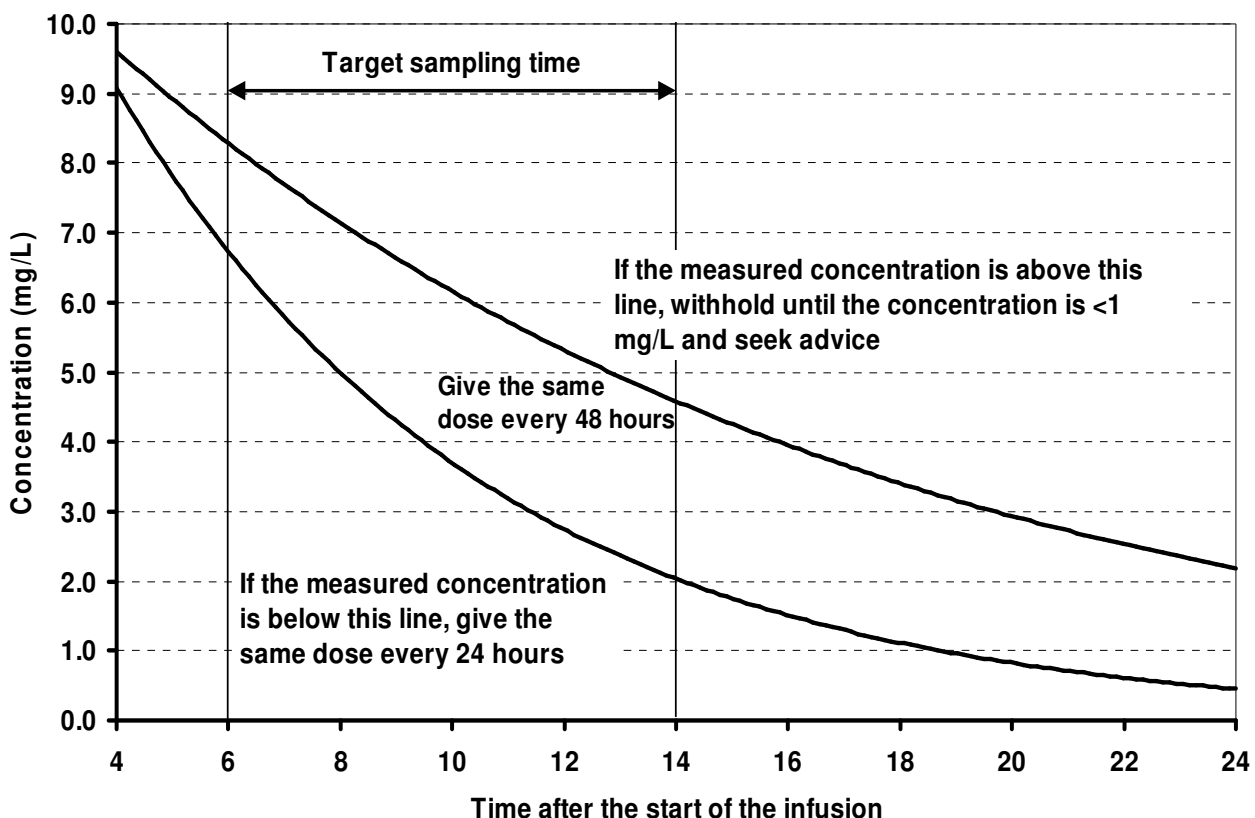
Weight → Creat Cl (ml/min) ↓	40 - 49 kg	50 - 59 kg	60 - 69 kg	70 - 80 kg	> 80 kg
< 21	2.5 mg/kg (max 180 mg) then take a sample after 24 hours				
21 - 30	180 mg 48 hourly	200 mg 48 hourly	240 mg 48 hourly	240 mg 48 hourly	260 mg 48 hourly
31 - 40	200 mg 48 hourly	240 mg 48 hourly	280 mg 48 hourly	300 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

Cautions

- Dose requirements will change if renal function alters – monitor serum creatinine daily.
- Review antimicrobial therapy daily. Seek advice from microbiology if gentamicin is required empirically for >48 - 72 hours.
- Stop after a maximum of 5 – 7 days unless there is a clear clinical and microbiological need for prolonged therapy.
- If the patient weighs less than 40 kg and creatinine clearance is > 20 ml/min, give a single dose of 5 mg/kg then take a sample 6 – 14 hours after the dose and plot on the graph.
- Seek advice from pharmacy or microbiology if you are unsure what to do.

Monitoring of gentamicin concentrations

- **Concentrations are meaningless unless the dose and sample time are recorded accurately.**
- Take a sample 6 – 14 hours after the start of the first infusion. Record the time of the dose and the blood sample on the request form and sample time on the sample tube.
- Plot the concentration measurement on the graph.
- This will indicate one of 3 options: 1) continue the present dosage regimen
2) adjust the dosage interval
3) withhold and resample after 24 hours
- Seek advice from pharmacy or microbiology if you are unsure how to interpret the result.
- If a blood sample is not taken, is lost or is taken at wrong time - if there is any concern about the patient's renal function, take a sample at 20-24 hours and wait for the result before giving the next dose. Otherwise take a blood sample after the next dose.
- Take a further sample 6-14 hours post dose, every 2 – 3 days.
- If the **concentration is unexpectedly high, or if renal function alters**, daily sampling may be necessary.



Appendix 3 GENTAMICIN POLICY (Hartford)

Initial dose of 7 mg/kg to a maximum of 600 mg

Dosage

- Check creatinine clearance using an on-line calculator or use the Cockcroft and Gault equation.
- If creatinine clearance is > 20 ml/min calculate the required dose at 7 mg/kg body weight and round this to the nearest 40 mg for ease of administration.
- In obese patients (>20% over Ideal Body Weight) calculate the dose using corrected dosing weight = ideal body weight + 0.4 (actual body weight – ideal body weight). See appendix 4 for a table of ideal body weight.
- For patients with creatinine clearance ≤ 20 ml/min, firstly confirm that gentamicin is the most appropriate treatment, and then calculate initial dosage using 2.5 mg/kg (maximum 180 mg) using actual weight or corrected dosing weight if obese (>20% over Ideal Body Weight). Alternatively, a single dose of 7 mg/kg may be considered.
- Administer as an infusion in 100 ml sodium chloride 0.9% or glucose 5% over 1 hour and ensure the time of administration is noted on the medicine chart.

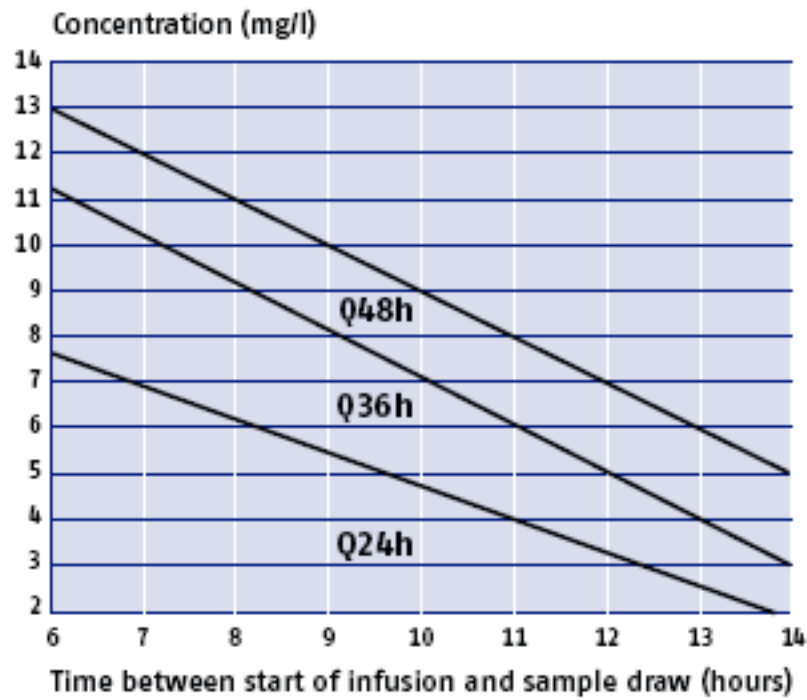
Cautions

- Dose requirements will change if renal function alters – monitor serum creatinine daily.
- Review antimicrobial therapy daily. Seek advice from a Microbiologist or ID Consultant if gentamicin is required empirically for >72 hours.
- Stop after a maximum of 5 – 7 days unless there is a clear clinical and microbiological need for prolonged therapy.

Monitoring of gentamicin concentrations

- **Concentrations are meaningless unless the dose and sample time are recorded accurately.**
- For patients with creatinine clearance > 20 ml/min, take a sample 6 – 14 hours after the start of the first infusion. Record the time of the dose and the blood sample on the request form and sample time on the sample tube.
- Plot the concentration measurement on the Hartford nomogram.
- This will indicate whether the dose should be repeated at 24, 36 or 48 hour intervals.
- Seek advice from pharmacy or microbiology if you are unsure how to interpret the result.
- Take a further sample 6-14 hours post dose, every 2 – 3 days. For patients on 36 or 48 hourly dosing, a gentamicin level should be checked after every infusion.
- For patients with creatinine clearance ≤ 20 ml/min, take a sample 24 hours after the start of the first infusion. Only give the next dose if the concentration is <1 mg/L. If it is >1mg/L withhold the dose and recheck in 12–24 hours.
- If a blood sample is not taken, is lost or is taken at wrong time - if there is any concern about the patient's renal function, take a sample at 20-24 hours and wait for the result. Only give the next dose if the concentration is <1 mg/L. If it is >1 mg/L withhold the dose and recheck in 12–24 hours.

- If the **concentration is unexpectedly high, or if renal function alters**, daily sampling may be necessary.



Appendix 4 - IDEAL BODY WEIGHT TABLES

These tables can be used to estimate a patient's ideal body weight and to calculate gentamicin dosing weight in patients classed as obese (>20% over Ideal body weight) when using the Hartford policy.

Females

Height Feet	5'	5'1"	5'2"	5'3"	5'4"	5'5"	5'6"	5'7"	5'8"	5'9"	5'10"	5'11"	6'	6'1"	6'2"	6'3"	6'4"
Height Inches	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76
Height cm	152	155	157	160	163	165	168	170	173	175	178	180	183	185	188	190	193
IBW kg	45.5	47.8	50.1	52.4	54.7	57	59.3	61.6	63.9	66.2	68.5	70.8	73.1	75.4	77.7	80	82.3

Males

Height Feet	5'	5'1"	5'2"	5'3"	5'4"	5'5"	5'6"	5'7"	5'8"	5'9"	5'10"	5'11"	6'	6'1"	6'2"	6'3"	6'4"
Height Inches	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76
Height cm	152	155	157	160	163	165	168	170	173	175	178	180	183	185	188	190	193
IBW kg	50	52.3	54.6	56.9	59.2	61.5	63.8	66.1	68.4	70.7	73	75.3	77.6	79.9	82.2	84.5	86.8

Appendix 5 – MAXIMUM BODY WEIGHT TABLE

This table can be used to determine whether patients are classed as obese (> 20% over ideal body weight) and to determine the maximum body weight for use in the Cockcroft-Gault equation.

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

Maximum body weight table			
Height (ft inches)	Height (cm)	MBW (kg) (male)	MBW (kg) (female)
4' 8"	142	49	43
4' 9"	145	52	47
4' 10"	147	54	49
4' 11"	150	58	52
5' 0"	152	60	55
5' 1"	155	62	58
5' 2"	158	66	60
5' 3"	160	68	62
5' 4"	163	71	66
5' 5"	165	74	68
5' 6"	168	77	71
5' 7"	170	79	74
5' 8"	173	82	77
5' 9"	175	85	79
5' 10"	178	88	82
5' 11"	180	90	85
6' 0"	183	94	88
6' 1"	185	96	90
6' 2"	188	98	94
6' 3"	191	101	-
6' 4"	193	104	-
6' 5"	195	107	-
6' 6"	198	109	-
6' 7"	201	113	-
6' 8"	203	115	-