Whittington Health NHS

Vancomycin and Teicoplanin Dosing in Adult Patients - Guideline

Subject:	Vancomycin and Teicoplanin Dosing in Adults
Policy Number	
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Policy Executive Owner:	Dr Julie Andrews (Consultant Microbiologist and Associate Medical Director for Patient Safety and Quality Improvement)
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Name of Assurance Committee:	Antimicrobial Steering Group (ASG)
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Target Audience:	All clinical staff involved in prescribing, dispensing and administering antibiotics i.e. Doctors, Nurses and Pharmacists.
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Version Control Sheet

Version	Date	Author	Status	Comment
2.0	May 2012	Ai-Nee Lim (Lead Pharmacist, Antimicrobials)	In-active	Higher target trough level for pneumonia, bacteraemia, infective endocarditis and osteomyelitis.
3.0	October 2015	Ai-Nee Lim (Lead Pharmacist, Antimicrobials)	In-active	Placed on new template.
4.0	March 2016	Ai-Nee Lim (Lead Pharmacist, Antimicrobials) **Contributors:** Dr Trupti Patel (SpR Infectious Diseases/ Microbiology) Dr M Kelsey (Consultant Microbiologist) Dr Julie Andrews (Consultant Microbiologist)	In-active	Significant changes in vancomycin dosing regimen with the addition of loading doses. This is based on a published study by Thomson et al (2009). Teicoplanin dosage and monitoring guide updated to reflect changes in the Summary of Product Characteristics.
5.0	September 2018	Ai-Nee Lim (Lead Pharmacist, Antimicrobials) **Contributors:** Dr M Kelsey (Consultant Microbiologist) Dr Julie Andrews (Consultant Microbiologist) Dr Trupti Patel (Consultant Microbiologist) Jonathan Flor (Medicines Information Pharmacist) Rebecca Chennells (Care of Older People Specialist Pharmacist)	Active	Guidance on estimating renal functions in patient who falls outside the normal patient population.

Abbreviations

CrCl	Creatinine Clearance (according to Cockcroft and Gault equation – see Appendix 1)
G5%	Glucose 5%
IM	Intramuscular
IV	Intravenous
N/S	Normal saline (i.e. sodium chloride 0.9%)
OPAT	Outpatient Parenteral Antimicrobial Therapy

➢ Criteria for use

This guideline provides guidance on glycopeptide (vancomycin and teicoplanin) prescribing, therapeutic drug monitoring and administration for adult patients (> 18 years old).

NOTE: This guideline must **not** be used to guide antimicrobial surgical prophylaxis therapy (see separate Surgical Antimicrobial Prophylaxis Guideline) and teicoplanin three times a week therapy for Outpatient Parenteral Antimicrobial Therapy (OPAT) (see separate Teicoplanin Three Times a Week Dosing and Monitoring for Adults - OPAT Guideline).

➢ Background

Factors to consider when prescribing glycopeptides (vancomycin and teicoplanin):

Indication:

- Vancomycin is the first-line glycopeptide at the Whittington Hospital.
- Teicoplanin is restricted for use in antimicrobial surgical prophylaxis, outpatient parenteral antimicrobial therapy (OPAT) or on the advice of Microbiology.

Renal impairment:

- Glycopeptides are renally excreted.[16]
- Monitor renal function regularly. Maintenance doses are based on renal function and will need to be adjusted in renal impairment.[4, 5, 6, 16]
- In patients with unstable and worsening renal function, the drug level must be taken sooner e.g. daily or seek Microbiology or Pharmacy for advice. Withhold the next dose until the result is available, and then follow the dose adjustment instructions.
- In patients with normal or stable renal function, do not delay the next dose while waiting for the results.

Body weights:

- Loading doses are based on actual body weight (ABW) - even in patients who are outside the normal patient population such as overweight, amputees, paraplegic or quadriplegic etc. [3, 16]
  NB: Do not delay giving the loading dose while estimating the patient's renal function to calculate the maintenance dose.

Elderly patients:

- There is a natural decrement of glomerular filtration with increasing age. [30]
- Care is required when prescribing glycopeptides for elderly patients.[3, 30]

Therapeutic Drug Monitoring (TDM):

- TDM of glycopeptides is required to optimise therapy and to minimise the risk of toxicity.[3, 19, 20]
- Risk of toxicity is increased with prolonged high blood concentrations.[18, 30]
- Trough level monitoring is the most accurate and practical method for monitoring glycopeptides.[1, 21]
- Unlike vancomycin, teicoplanin assays are not performed in-house and the turnaround time is 2 – 3 days. Do not withhold doses of teicoplanin while waiting for assay results to be available unless otherwise advised by Microbiology. In patients with worsening renal function or highly unstable teicoplanin levels, please contact Microbiology or Pharmacy for dosing advice.

VANCOMYCIN INTRAVENOUS (IV) DOSING AND MONITORING

LOADING DOSE (initial STAT dose)		
Actual body weight (ABW)	**Vancomycin Dose**	**Dose Frequency**
< 40 kg	750mg	**STAT** observe time interval between loading dose & the first maintenance dose (see Dose Interval below)
40 – 59 kg	1000mg	
60 – 90 kg	1500mg	
> 90 kg	2000mg	

Seek pharmacy advice BEFORE prescribing for patients whom estimation of renal function using serum creatinine may be inaccurate:[32]

- Overweight (BMI > 25) – *see Appendix 2*
- Underweight (BMI < 18.5) – *see Appendix 3*
- Amputees – *see Appendix 4*
- Pregnancy
- Paraplegia or quadriplegia – *see Appendix 5*
- Rapidly changing kidney function

MAINTENANCE DOSE			TAKE LEVEL – Trough (pre-dose) level	
Creatinine Clearance* (mL/min)	**Vancomycin Dose**	**Dose Interval** (START TIME AFTER THE LOADING DOSE & FURTHER DOSING INTERVALS)	**Time of 1st drug level monitoring** (including loading dose)	**Frequency of drug level monitoring**
> 110	1500mg	12 hourly	Before 4th dose	If stable renal function: **TWICE WEEKLY** Give the next dose. Do not wait for the results. If **WORSENING** renal function: **DAILY** or **AS ADVISED** Withhold dose until result is available then follow instruction under Dose Adjustment.
90 – 110	1250mg	12 hourly	Before 4th dose	
75 – 89	1000mg	12 hourly	Before 4th dose	
55 – 74	750mg	12 hourly	Before 4th dose	
40 – 54	500mg	12 hourly	Before 4th dose	
30 – 39	750mg	24 hourly	Before 3rd dose	
20 – 29	500mg	24 hourly	Before 3rd dose	
10 – 20	500mg	48 hourly	Before 2nd dose	
< 10	500mg	48 hourly (check level before giving)	24-hour intervals	**24-hour intervals** Withhold dose if level is high and adjust dose / dosage interval accordingly.
CRRT Continuous renal replacement therapy	Withhold initiating maintenance dose until level is in range. Maintenance dose can range between 500 – 1500mg 24hrly. Adjust the dose or dosage interval to achieve the target range.		24-hour intervals	

* Creatinine Clearance (CrCl) based on Cockcroft and Gault equation - see Appendix 1 or 'Clearance calculator' on MicroGuide® mobile app.

TROUGH (PRE-DOSE) LEVEL: Aim for **10 – 15 mg/L** (or **15 – 20mg/L** for pneumonia, bacteraemia, infective endocarditis, osteomyelitis or less sensitive strains of MRSA).

Vancomycin assays must be collected in **6ml red top vacutainer tube** (serum sample). On **weekends**, samples must arrive in the Microbiology laboratory no later than 11am. For out-of-hours, please contact the on-call SpR in Microbiology via switchboard.

Dose Adjustment – always check whether the level is a TRUE trough before interpreting the result.		
Trough Level	**Vancomycin Maintenance Dose Adjustment**	**Recheck Level**
< 5 mg/L	Move up 2 dose bands from current dosing schedule.	If dose adjustment undertaken: Take a level **BEFORE** the **4th dose** (if 12hrly dosing) **or 3rd dose** (if 24hrly dosing) **or 2nd dose** (if 48hrly dosing) of the new dosage regimen. OR Re-check earlier, if **worsening** renal function. If level is within range and is stable: **TWICE WEEKLY**
5 – 9 mg/L	Move up 1 dose band from current dosing schedule.	
10 – 15 mg/L	**If the patient is responding:** Maintain the present dosage regimen. **If the patient is seriously ill (severe or deep-seated infection):** Move up 1 dose banding from current dosing schedule - to achieve a trough level of 15 – 20 mg/L.	
15 – 20 mg/L	Maintain the present dosage regimen.	
21 – 25 mg/L	Move down 1 dose band without omitting any doses.	
26 – 30 mg/L	Omit next dose AND decrease by 2 dose bands from current dosing schedule.	
> 30mg/L	Omit further doses until level is ≤20 mg/L. Seek Microbiology advice.	

TEICOPLANIN (STANDARD DOSING REGIMEN)

INTRAVENOUS (IV) DOSING AND MONITORING

*** Teicoplanin is the 2nd-line glycopeptide and should ONLY be used on the advice of Microbiology. ***

1. Is the teicoplanin for **surgical prophylaxis** OR **acute treatment**?

Prophylaxis → Refer to the Antimicrobial Surgical Prophylaxis Therapy Guideline Surgical Antimicrobial Prophylaxis Guideline.

Treatment

2. Does the patient fulfil the criteria for **3 x weekly** teicoplanin dosing for **OPAT** administration?

YES → Refer to the Teicoplanin Three Times a Week Therapy for Outpatient Parenteral Antimicrobial Therapy (OPAT) Teicoplanin 3 x Weekly OPAT Guideline.

NO

3. Is the teicoplanin for **DEEP SEATED** infection e.g. bone & joint infection or infective endocarditis?

YES →

NOTE: Teicoplanin is not licensed to be used for longer than 4 months.

NO

4. Is the teicoplanin for **NON-DEEP SEATED** infection e.g. skin and soft tissue infections?

YES →

BONE & JOINT INFECTION / INFECTIVE ENDOCARDITIS

TROUGH (PRE-DOSE) aim for **> 20mg/L** but < 60mg/L

Actual body weight	LOADING DOSE (12mg/kg 12 hourly for 3 doses)	MAINTENANCE DOSE* (12mg/kg ONCE a day)
≥157kg	2000mg 12 hourly for 3 doses	2000mg once a day
140 - 156kg	1800mg 12 hourly for 3 doses	1800mg once a day
125 - 139kg	1600mg 12 hourly for 3 doses	1600mg once a day
105 - 124kg	1400mg 12 hourly for 3 doses	1400mg once a day
90 - 104kg	1200mg 12 hourly for 3 doses	1200mg once a day
75 – 89kg	1000mg 12 hourly for 3 doses	1000mg once a day
60 - 74kg	800mg 12 hourly for 3 doses	800mg once a day
45 - 59kg	600mg 12 hourly for 3 doses	600mg once a day
≤ 44kg	400mg 12 hourly for 3 doses	400mg once a day

SKIN AND SOFT TISSUE INFECTIONS

TROUGH (PRE-DOSE) aim for **> 15mg/L** but < 60mg/L

Actual body weight	LOADING DOSE (6mg/kg 12 hourly for **3** doses)	MAINTENANCE DOSE* (6mg/kg ONCE a day)
≥145kg	1000mg 12 hourly for 3 doses	1000mg once a day
110 - 144kg	800mg 12 hourly for 3 doses	800mg once a day
75 - 109kg	600mg 12 hourly for 3 doses	600mg once a day
45 - 74kg	400mg 12 hourly for 3 doses	400mg once a day
≤ 44kg	200mg 12 hourly for 3 doses	200mg once a day

* If renal impairment [14, 16, 31]

After the **4th day** of treatment:

CrCl	Dose reduction
40 – 60 ml/min	Give normal dose for weight every **48 hours**.
< 40 ml/min or if undergoing renal replacement therapy	Give normal dose for weight every **72 hours**.

MONITOR LEVELS. Take TROUGH level (i.e. immediately prior to giving a dose) around the 6th or 7th dose (including loading dose). Then ONCE a week thereafter.

Teicoplainin assays are sent away with a turnaround time of 2 – 3 days. Do NOT withhold doses pending results.

Dose adjustment (always check whether level is a TRUE trough before interpreting the result)

Trough level	Teicoplanin dose adjustment	
	DEEP SEATED	NON-DEEP SEATED
< 10 mg/L	Move up 1 dose band and re-load with the new dose.	Repeat loading dose. Maintain with the normal dose.
10 – 15 mg/L	Repeat loading dose. Maintain with the normal dose.	Increase maintenance dose by 200mg.
16 – 19 mg/L	Increase maintenance dose by 200mg.	No changes required.
20 – 40 mg/L	No changes required.	No changes. Monitor CrCl regularly.
45 – 60 mg/L	Recheck CrCl. Consider reducing maintenance dose depending on drug level & renal function*.	Recheck CrCl. Consider reducing maintenance dose depending on drug level & renal function*.
> 60 mg/L	Do not give a further dose. Seek Microbiology advice.	Do not give a further dose. Seek Microbiology advice.

IV ADMINISTRATION INSTRUCTION: For doses ≤ 800mg, give as an IV bolus over 4 – 5 minutes.
For doses > 800mg (or > 12mg/kg), dilute in 100ml N/S or G5% and give as a slow IV infusion over 60 minutes.[9]

Appendix 1: Creatinine Clearance (CrCl) - using Cockcroft and Gault equation

For both vancomycin and teicoplanin, renal function must be estimated according to the creatinine clearance based on the Cockcroft and Gault equation.[1]

Creatinine Clearance (CrCl) using Cockcroft and Gault equation:

$$\text{CrCl (ml/min)} = \frac{(140 - \text{age}) \times \text{*}\textbf{Actual Body Weight (kg)} \times 1.23 \text{ (male) OR } 1.04 \text{ (female)}}{\text{Serum creatinine (µmol/L)}}$$

* Actual Body Weight should only be used in normal weight patients i.e. BMI between 18.5 and 25. For patients who fall outside the normal patient population, see Appendix 2 to 5.

NOTE: The Creatinine Clearance (CrCl) calculator is available on the MicroGuide® mobile app.

Creatinine is a product of muscle breakdown which is produced at a constant rate and is almost exclusively cleared through the glomerular filtration.[45] Creatinine clearance (CrCl) is therefore used as an estimate of glomerular filtration rate (GFR). [45, 47]

Limitations

There are limitations to the use of CrCl. Serum creatinine levels are dependent on muscle mass and diet, therefore estimates should be interpreted with caution in certain individuals e.g. patients with muscle-wasting disorders, limb amputation, extremes of weight, or vegans etc. [47]

Creatinine-derived measurements are also not useful in periods of rapidly changing renal function or in patients with acute kidney injury (AKI). [47]

Appendix 2: Overweight

Creatinine production is determined by lean muscle mass.
If the patient is clinically obese (i.e. BMI > 25 or > 20% over IBW), use ideal body weight (IBW) to estimate the creatinine clearance.

STEP 1: **Determine the Ideal Body Weight (IBW) - using the Devine formula:**

IBW (male) = 50kg + [0.91 x (height in cm - 152.4)]
IBW (female) = 45.5 kg + [0.91 x (height in cm - 152.4)]

Table 1: Quick guide to determine IBW based on patient's height:

Ideal body weight (IBW) chart:			
HEIGHT		**IDEAL BODY WEIGHT (kg)**	
Feet OR	**cm**	**Male ♂**	**Female ♀**
5ft 1in	155	**52.3**	**47.8**
5ft 2in	158	**54.6**	**50.1**
5ft 3in	160	**56.9**	**52.4**
5ft 4in	163	**59.2**	**54.7**
5ft 5in	165	**61.5**	**57.0**
5ft 6in	168	**63.8**	**59.3**
5ft 7in	170	**66.1**	**61.6**
5ft 8in	173	**68.4**	**63.9**
5ft 9in	175	**70.7**	**66.2**
5ft 10in	178	**73.0**	**68.5**
5ft 11in	180	**75.3**	**70.8**
6ft 0in	183	**77.6**	**73.1**
6ft 1in	185	**79.9**	**75.4**
6ft 2in	188	**82.2**	**77.7**
6ft 3in	191	**84.5**	**80.0**
6ft 4in	193	**86.8**	**82.3**
6ft 5in	196	**89.1**	**84.6**
6ft 6in	198	**91.4**	**86.9**
6ft 7in	201	**93.7**	**89.2**
6ft 8in	203	**96.0**	**91.5**
6ft 9in	206	**98.3**	**93.8**
6ft 10in	208	**100.6**	**96.1**
6ft 11in	211	**102.9**	**98.4**

STEP 2: **Calculate the Creatinine Clearance using the Ideal Body Weight (IBW):**

CrCl (ml/min) = (140 – age) x **Ideal Body Weight (kg)** x 1.23 (male) OR 1.04 (female)
* Serum creatinine (micromol/L)

Appendix 3 – Underweight

In underweight patients, a low serum creatinine is usually reflective of a decreased muscle mass rather than an increased rate of renal elimination.

If the patient is clinically underweight (i.e. BMI < 18.5 or at least 10% below IBW), the patient's Cockcroft & Gault creatinine clearance must be multiplied by an adjustment factor (AF) of 0.69. [45]

STEP 1: **Calculate creatinine clearance (CrCl) using Cockcroft and Gault equation**:

$$\text{CrCl (ml/min)} = \frac{(140 - \text{age}) \times \textbf{Actual Body Weight (kg)} \times 1.23 \text{ (male) OR } 1.04 \text{ (female)}}{\text{* Serum creatinine (micromol/L)}}$$

STEP 2: **Multiply the CrCl by an adjustment factor of 0.69 (= CrCl $_{\text{Adjustment Factor}}$):** [45]

$$\text{CrCl}_{\text{Adjustment Factor}} = \text{CrCl} \times 0.69$$

Appendix 4 – Amputees

Amputees have lower serum creatinine due to the loss of muscle mass. The Amputation IBW, which takes into account the percentage estimated body weight loss (% EBWL), must be used to calculate the creatinine clearance: [38]

STEP 1: **Identify the Percentage Estimated Body Weight Loss (% EBWL):** [38, 44]

If the patient has lost multiple limbs, sum all the respective % EBWL.

Level of amputation (Unilateral)	% EBWL
Hand – Partial	0.35%
Hand – Entire	0.7%
Elbow – Below elbow	1.5%
Elbow – Above elbow	3.65%
Arm – Entire (up to the shoulder joint) [44]	4.9%
Foot – Partial	0.75%
Foot – Entire	1.5%
Knee – Below knee	3.7%
Knee – Above knee	10.94%
Knee disarticulation (up to the knee joint)	4.4%
Hip disarticulation (up to the hip joint)	16%

STEP 2: **Calculate Amputation Ideal Body Weight (Amputation IBW):** [38]

$$\textbf{Amputation IBW (kg)} = \frac{(100 - \textbf{\% EBWL})}{100} \times \textbf{Ideal Body Weight}$$

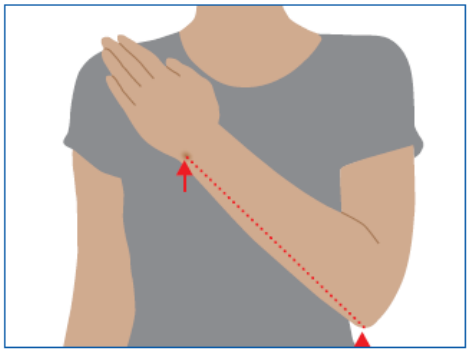
Ideal Body Weight (kg):

IBW (male) = 50kg + [0.91 x (pre-amputation height* in cm - 152.4)]

IBW (female) = 45.5 kg + [0.91 x (pre-amputation height* in cm - 152.4)]

* If pre-amputation height is unknown i.e. cannot be measured or no documentation, height may be estimated from the **(i) forearm (ulna) length** or **(ii) knee height** as below: [44]

(i) Length of forearm (ulna)

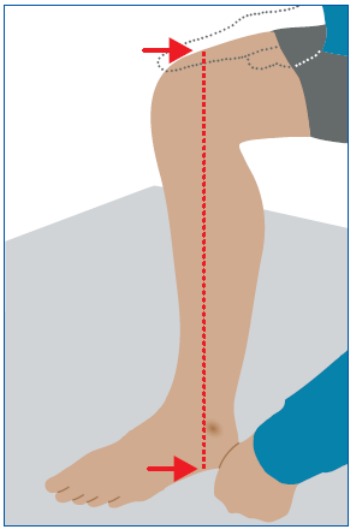


- Ask subject to bend an arm (left side if possible), palm across chest, fingers pointing to opposite shoulder.
- Using a tape measure, measure the length in centimetres (cm) to the nearest 0.5 cm between the point of the elbow (olecranon) and the mid-point of the prominent bone of the wrist (styloid process).
- Use the table on page 12 to convert ulna length (cm) to height (m).

Table 5 Estimating height from ulna length

Height (m)	Men (<65 years)	1.94	1.93	1.91	1.89	1.87	1.85	1.84	1.82	1.80	1.78	1.76	1.75	1.73	1.71
	Men (≥65 years)	1.87	1.86	1.84	1.82	1.81	1.79	1.78	1.76	1.75	1.73	1.71	1.70	1.68	1.67
	Ulna length (cm)	32.0	31.5	31.0	30.5	30.0	29.5	29.0	28.5	28.0	27.5	27.0	26.5	26.0	25.5
Height (m)	Women (<65 years)	1.84	1.83	1.81	1.80	1.79	1.77	1.76	1.75	1.73	1.72	1.70	1.69	1.68	1.66
	Women (≥65 years)	1.84	1.83	1.81	1.79	1.78	1.76	1.75	1.73	1.71	1.70	1.68	1.66	1.65	1.63
Height (m)	Men (<65 years)	1.69	1.67	1.66	1.64	1.62	1.60	1.58	1.57	1.55	1.53	1.51	1.49	1.48	1.46
	Men (≥65 years)	1.65	1.63	1.62	1.60	1.59	1.57	1.56	1.54	1.52	1.51	1.49	1.48	1.46	1.45
	Ulna length (cm)	25.0	24.5	24.0	23.5	23.0	22.5	22.0	21.5	21.0	20.5	20.0	19.5	19.0	18.5
Height (m)	Women (<65 years)	1.65	1.63	1.62	1.61	1.59	1.58	1.56	1.55	1.54	1.52	1.51	1.50	1.48	1.47
	Women (≥65 years)	1.61	1.60	1.58	1.56	1.55	1.53	1.52	1.50	1.48	1.47	1.45	1.44	1.42	1.40

(ii) Knee height



- Measure left leg if possible.
- The subject should sit on a chair, without footwear, with knee at a right angle.
- Hold tape measure between 3rd and 4th fingers with zero reading underneath fingers.
- Place your hand flat across the subject's thigh, about 4 cm (1½ inches) behind the front of the knee.
- Extend the tape measure straight down the side of the leg in line with the bony prominence at the ankle (lateral malleolus) to the base of the heel. Measure to nearest 0.5 cm.
- Note the length and use the table on page 13 to convert knee height (cm) to height (m).

Table 6 Estimating height from knee height

Height (m)	Men (18-59 years)	1.94	1.93	1.92	1.91	1.90	1.89	1.88	1.87	1.865	1.86	1.85	1.84	1.83	1.82	1.81
	Men (60-90 years)	1.94	1.93	1.92	1.91	1.90	1.89	1.88	1.87	1.86	1.85	1.84	1.83	1.82	1.81	1.80
	Knee height (cm)	65.0	64.5	64.0	63.5	63.0	62.5	62.0	61.5	61.0	60.5	60.0	59.5	59.0	58.5	58.0
Height (m)	Women (18-59 years)	1.89	1.88	1.875	1.87	1.86	1.85	1.84	1.83	1.82	1.81	1.80	1.79	1.78	1.77	1.76
	Women (60-90 years)	1.86	1.85	1.84	1.835	1.83	1.82	1.81	1.80	1.79	1.78	1.77	1.76	1.75	1.74	1.73
Height (m)	Men (18-59 years)	1.80	1.79	1.78	1.77	1.76	1.75	1.74	1.73	1.72	1.71	1.705	1.70	1.69	1.68	1.67
	Men (60-90 years)	1.79	1.78	1.77	1.76	1.74	1.73	1.72	1.71	1.70	1.69	1.68	1.67	1.66	1.65	1.64
	Knee height (cm)	57.5	57.0	56.5	56.0	55.5	55.0	54.5	54.0	53.5	53.0	52.5	52.0	51.5	51.0	50.5
Height (m)	Women (18-59 years)	1.75	1.74	1.735	1.73	1.72	1.71	1.70	1.69	1.68	1.67	1.66	1.65	1.64	1.63	1.62
	Women (60-90 years)	1.72	1.71	1.70	1.69	1.68	1.67	1.66	1.65	1.64	1.63	1.625	1.62	1.61	1.60	1.59
Height (m)	Men (18-59 years)	1.66	1.65	1.64	1.63	1.62	1.61	1.60	1.59	1.58	1.57	1.56	1.555	1.55	1.54	1.53
	Men (60-90 years)	1.63	1.62	1.61	1.60	1.59	1.58	1.57	1.56	1.55	1.54	1.53	1.52	1.51	1.49	1.48
	Knee height (cm)	50.0	49.5	49.0	48.5	48.0	47.5	47.0	46.5	46.0	45.5	45.0	44.5	44.0	43.5	43.0
Height (m)	Women (18-59 years)	1.61	1.60	1.59	1.585	1.58	1.57	1.56	1.55	1.54	1.53	1.52	1.51	1.50	1.49	1.48
	Women (60-90 years)	1.58	1.57	1.56	1.55	1.54	1.53	1.52	1.51	1.50	1.49	1.48	1.47	1.46	1.45	1.44

STEP 3: **Calculate the Creatinine Clearance using the Amputation IBW:**

Creatinine Clearance, CrCl (ml/min)

$$= \frac{(140 - \text{age}) \times \textbf{Amputation IBW} \times 1.23 \text{ (male) OR } 1.04 \text{ (female)}}{\text{Serum creatinine (micromol/L)}}$$

If patient's Actual Body Weight (ABW) is less than the Amputation IBW, use ABW to calculate CrCl.

Appendix 5 – Muscle / Neurological disorders (including Paraplegia & Quadriplegia)

Patients with neurological or muscle disorder have reduced muscle mass due to chronic immobility and muscle wasting, resulting in significantly lower serum creatinine (Quadriplegics < Paraplegics). Both Cockcroft-Gault (CrCl) and MDRD (eGRF/1.73m^2) equations would grossly overestimate creatinine clearance by more than 40%.

For drug dosing, the recommended equation to estimate renal function is the "Spinal Cord Injury Equation" creatinine clearance (CL_{SCI}): [33, 34, 35, 36]

STEP 1: **Calculate the "modified" Cockcroft & Gault creatinine clearance ($CrCl_{Modified}$)**: [33, 34]

$$CrCl_{Modified} = \frac{(140 - age) \times {}^{\ddagger} \text{Ideal Body Weight (kg)} \times 1.23 \text{ (male) OR } 1.04 \text{ (female)}}{* \text{ Serum creatinine (micromol/L)}}$$

* If serum creatinine:

- **LESS than** 88.89 micromol/L = use **88.89 micromol/L** as the serum creatinine
- **EQUALS** to or **MORE** than 88.89 micromol/L = use **actual** serum creatinine

‡ Ideal Body Weight (kg) = [0.91 x (height in cm - 152.4)] + 50kg (male) or 45.5 kg (female).

If patient's Actual Body Weight (ABW) is less than the Ideal Body Weight, use ABW to calculate $CrCl_{Modified}$.

STEP 2: **Estimate the creatinine clearance using the "Spinal Cord Injury Equation" (CL_{SCI})**: [33, 34]

$$CL_{SCI} = 2.3 \times (CrCl_{Modified})^{0.7}$$

Example:

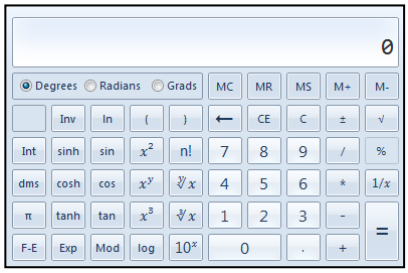
Calculate the creatinine clearance for a quadriplegic patient who is a 27 years old male, underweight weighing 43kg, and has a serum creatinine of 37 micromol/L.

$$CL_{Modified\ Cockcroft\text{-}Gault} = \frac{(140 - 27 \text{ years old}) \times 43\text{kg} \times 1.23 \text{ (male)}}{\mathbf{88.89} \text{ micromol/L}} = 67.23 \text{ ml/min}$$

$CL_{SCI} = 67.23^{0.7} \times 2.3$

= 67.23 | x^y | 0.7 | * | 2.3

= **43.75** ml/min



Therefore, the estimated creatinine clearance is 43.75 ml/min.

Appendix 6

Both vancomycin and teicoplanin bactericidal activities are dependent on the total amount of drug exposure above the minimum inhibitory concentration over a 24-hour period (AUC_{24}/MIC).

Vancomycin

- Vancomycin has an elimination half-life of 6 – 12 hours [Kucer's].
- For vancomycin therapy to be optimal an adequate trough concentration must be maintained. Patients whose trough concentrations are maintained at ≥10mg/L are more likely to become afebrile and have a normal white blood cell count within 72 hours [Zimmerman et al 1995].
- Routine measurement of peak concentrations is NOT advocated because:
  - **Bactericidal activity is concentration-independent.**

    Peak concentrations have not been proven to be predictive of either clinical outcome or toxicity [Saunders 1995, Larsson 1996].
  - **Trough levels sufficiently predict peak levels.**

    Peak vancomycin concentration has been shown not to exceed 40mg/L as long as the trough concentrations do not exceed 15mg/L [Saunders 1994]. Reversible ototoxicity is generally observed at concentrations exceeding 40mg/L.
  - **Trough levels can predict renal function deterioration.**

    Nephrotoxicity generally occurs at trough concentrations exceeding 20mg/L [Zimmerman et al 1995].
- Peak concentration may occasionally be useful, such as in severe infections requiring high concentrations to penetrate selected sites (e.g. endocarditis and osteomyelitis), in patients with altered volume of distribution (e.g. burns, ascites, pregnancy, significant oedema) or in patients who are not responding to therapy.
- In morbidly obese patients i.e. BMI ≥ 40kg/m^2 or > 90% overweight, serum clearance is at least double of that in non-obese patients. Doses should be based on Actual Body Weight (ABW) [Blouin et al 1982]. Shorter dosage intervals may be desirable to avoid high transient peak concentrations.
- Concomitant nephrotoxic agents are a major determinant for nephrotoxicity, with incidence rates reported of 43% versus < 5% with vancomycin alone [Saunders 1994, Rybak 1990].

Teicoplanin ⁑⁑ NOT the first-line glycopeptide therapy ⁑⁑

- Teicoplanin has a long serum half-life of between 88 – 182 hours which reflects its large molecular size, high protein binding and extensive tissue distribution [Kucer's].
- The pharmacokinetics of teicoplanin is unpredictable with considerable inter-individual variability in the serum concentration of patients given the same doses [MacGowan et al 2004].
- Serum monitoring of teicoplanin is generally recommended to ensure therapeutic dosage. However, the relationship between serum concentration and toxicity has not been established [Wilson 1998, Wang 2015].
- For mild-to-moderate infection, there is little evidence to support serum monitoring unless abnormal renal clearance is anticipated e.g. in intravenous drug abusers, elderly or renally impaired patients [Wilson 1998, Darley et al 2004].
- In severe infections such as septicaemia, joint infection and endocarditis, the relationship between outcome and trough concentration is well documented. Serum monitoring should be used to optimise therapy [Darley et al 2004, Harding et al 2000].
- Higher incidences of side effects with teicoplanin, such as thrombocytopenia and elevated serum creatinine, have been associated with serum levels above 60mg/L [Wilson 1998]. Tinnitus or a mild loss of high-frequency hearing detected by audiograms has been noted in some patients receiving high-dose (15mg/kg/day) teicoplanin with trough levels of 41 mg/L [Kucer's online].
- Teicoplanin is 90% bound to plasma protein (albumin). In hypoalbuminaemia, teicoplanin is more rapidly distributed and cleared, which may result in lower teicoplanin levels [Pea 2001].

➢ Contacts

During working hours (Monday to Friday, 09:00 – 17:00)

SpRs in Microbiology	ext. 5085 or 5780; bleep 3069
Consultant Microbiologist	ext. 5082 or 3894 or 3197
Lead Pharmacist, Antimicrobials	ext. 3732; bleep 3138

Out of hours

On-call SpR in Microbiology	Via Whittington switchboard
On-call pharmacist	Via Whittington switchboard

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Systematic review of studies published from 1980 to April 2013. For obese patients, ideal body weight (IBW) underestimates creatinine clearance (CrCl) and total body weight (TBW) overestimates CrCl. Some studies suggest that adjusted body weight with a factor of 0.4 is most accurate, while others suggest the use of lean body weight. These studies have failed to produce a definitive resolution to the controversy. Despite many well-designed studies, the Cockcroft-Gault body weight controversy remains unresolved and uncertainty continues to exist as to which form of weight should be used in the equation. It is propose the use of a CrCl range for drug dosing purposes, with the lower boundary defined by using IBW in the Cockcroft-Gault equation and the upper boundary by using TBW.

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To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with and effectiveness of the document?	Yes	

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10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Assess/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report ? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	**Lead**	**Tool**	**Frequency**	**Reporting arrangements**
Appropriate usage, dosing and monitoring of teicoplanin and vancomycin	Respective speciality team supported by the Microbiology & Pharmacy Department.	In-house audit tool	Annual audit and report.	• Respective departmental meeting • Antimicrobial Steering Group