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Therapeutic Drug Monitoring (TDM) protocol for adult

Vancomycin and Aminoglycosides

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2019

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Table of content:

1. **Purpose:**
   To establish a standardized pharmacokinetic approach for patient receiving drugs that are routinely monitored utilizing serum drug concentration at MOH hospitals.

2. **Definition**

   TDM: Therapeutic Drug Monitoring.

3. **Functions Affected**
   Clinical Pharmacist Specialist, Staff Pharmacists, Pharmacy Resident and Pharmacy Student.

4. **Policy:**

4.1. The Pharmacy Department has Therapeutic Drug Monitoring (TDM) service, using the latest and most updated MOH guidelines.

4.2. The Pharmacist in-charge of the service is a qualified pharmacist.

4.3. The TDM is the use of drug concentration measurements in body fluids as an aid to the management of drug therapy for the cure, alleviation, or prevention of disease.

4.4. The TDM service guidelines were developed to ensure safe and efficacious dosage regimens through the application of pharmacokinetic/pharmacodynamics principles and determination of drug serum concentrations.

4.5. The policy/procedure manual outlines standard guidelines which should be followed when providing clinical pharmacokinetic monitoring of the following drugs: aminoglycosides and vancomycin.

4.6. Educating pharmacists, physicians, nurses, and other clinical practitioners on pharmacokinetic principles and/or appropriate indications for clinical pharmacokinetic monitoring.

5. **Procedures:**

5.1 Therapeutic drug monitoring testing will be initiated by the ordering provider or Pharmacy Department.

5.2 Upon receiving order for pharmacy to dose a specific medication, a pharmacist will assess the patient and collect relevant information necessary to appropriately dose/monitor the specified drug so as to achieve therapeutic drug levels and minimize any potential risks of toxicity. Such items of information may include. But not are limited to:

a. Indication for therapy (i.e. type and site of infection for antibiotic dosing/monitoring consults).
b. Age.
c. Gender.
d. Height/Weight.
e. Renal/Hepatic function.
f. Estimated pharmacokinetic parameters.
g. Medication history.
h. Current/last known serum drug concentration.

5.3 The order should include the drug to be tested and, at minimum, the relative time when the sample should be drawn (peak, trough, random). Whenever possible, an exact time should be entered to correlate with drug administration time.

5.4 Once all patient information, laboratory and clinical data completed, the pharmacist in-charge start to follow sample guidelines and medication monitoring guidelines (Attached) to monitoring medication level, patient situation and follow-up the patient during therapy duration.

5.5 Laboratory and nursing staff will work together to determine the optimum time for specimen collection. For TDM to be meaningful, the patient should be in steady-state on the present dose of the drug. In general, samples should be taken after drug dosing has continued for at least four half-lives.

5.6 Unless otherwise specified, sampling times will utilize the following definitions:

a) Trough – Immediately before the next scheduled dose.
b) Peak – 1 Hour post dose (Time to peak may be used to determine alternative peak times).

5.7 In cases of suspected toxicity, waiting to attain steady-state is not necessary and a random drug level may be collected to aid in clinical decision making.

5.8 The laboratory department should deal with the drug level sample as urgent order and the result should be available in the system as soon as 1 – 2 hours maximum.

6. Responsibility:

6.1. TDM Pharmacist:

6.1.1. Responsible for receiving order from health care professionals or ordering and monitor the serum level during period of therapy and report it to the head of service and the physician responsible for the patient.
6.1.2. The working hours from 7:00 am-4:00 pm from Sunday to Thursday.
6.1.3. Responsible to monitor any new order & report it to the head of service and the physician responsible for the patient.

7. Equation:

7.1.1. Calculate creatinine clearance with the Cockcroft-Gault equation using an ideal body weight (IBW) or an adjusted body weight (ABW) if the patient is obese
7.1.2. CrCL (mL/min) = (140 – age) x IBW / SCr x 72 (x 0.85 for females)

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Vancomycin Dosing and Monitoring in Adult

Vancomycin is a glycopeptide antibiotic (time dependent) used intravenously for treatment of patients with suspected or proven invasive gram-positive infections, including methicillin-resistant Staphylococcus aureus (MRSA)

1.Dosing:

Loading (initial) dose

- Used in seriously ill patients (e.g. requiring intensive care) and patients with complicated infections (e.g. bacteremia, pneumonia, endocarditis, osteomyelitis, prosthetic joint infection and infections involving the central nervous system)
    - Recommended dose: 25-30 mg/kg IV (rounded to the nearest 250 mg increment)
    - Obese patients: up to a single maximum dose of 3 grams
- The dose usually calculated based on actual body weight (ABW)
- For obese patients, initial dosing can be based on ABW and then adjusted based on serum concentrations of vancomycin to achieve therapeutic levels

Maintenance dose

- Recommended dose:15-20 mg/kg IV Q8-12H (rounded to the nearest 250mg) (not to exceed 2 g per dose).
- In the setting of rapid clearance (such as in burn patients, in younger patients with normal renal function or obese), administration of vancomycin every 8 hours may be required to achieve target troughs

2.Monitoring:

Vancomycin level:

- Trough serum vancomycin concentrations are the most accurate and practical method for monitoring efficacy and safety (nephrotoxicity).
- For patients with normal renal function, it takes approximately 4 doses of vancomycin to reach steady state. Trough concentration should be drawn 30 minutes before the 4th dose.
- Trough concentrations may be drawn earlier in critically ill patients, patients with unstable renal function and patients on vancomycin dosing interval more than or equal 24 hours.

- Trough concentrations must be interpreted with caution since additional doses will accumulate until steady state is reached.

Renal function:

- Monitor renal function for nephrotoxicity three time per week and more frequently when vancomycin combined with another nephrotoxic drugs (aminoglycoside, furosemide, piperacillin-sulbactam…etc)
- Vancomycin-Induced Nephrotoxicity: A minimum of two or three consecutive documented increases in serum creatinine concentrations (defined as an increase of ≥ 0.5 mg/dL or a ≥50% increase from baseline, whichever is greater) after several days of vancomycin therapy or a drop in calculated CrCl of 50% from baseline on two consecutive days in the absence of an alternative explanation.

Infusion related reaction monitoring:

- Monitor for infusion related event, including hypotension and red man syndrome.
- Rapid IV administration (<60 minutes) may increase risk of red man syndrome and may result in hypotension, flushing, erythema , urticaria , pruritus and cardiac arrest.

CBC monitoring:

- Periodic monitoring for CBC should be done to screen for neutropenia and thrombocytopenia in patient with prolong vancomycin therapy or those whose receive concomitant drug that cause bone marrow suppression.

The target trough concentration depends on the type infection :

Type of Infection	Target Trough Concentration
Uncomplicated infection : Soft and skin tissue infectio [2,3]	10 – 15 mcg/ml
Complicated infection (Endocarditis , Osteomyletis , Bactermia , Prosthetic joint infection , pneumonia, Meningitis)	15 – 20mcg/ml

3. Dose adjustment:

The Adjustment of Vancomycin doses based on the level:

Note: Always check that the dosage history and sampling time are appropriate before interpreting the result.

Trough	Recommended Adjustment
< 5	- Decrease the dosage interval to the next frequency (example: every 12 hr to every 8 hr) - Or increase the total daily dose: • If goal is 10-15 mcg/mL ⇒ Increase dose by 25%

	• If goal is 15-20 mcg/mL⇒ Increase dose by 50 %
5-10	• If goal is 10-15 mcg/mL ⇒ Increase dose 25% • If goal is 15-20 mcg/mL⇒ decrease the dose interval to the next frequency or Increase every dose by 50%
10-15	• If goal is 10-15 mcg/mL ⇒ No change • If goal is 15-20 mcg/mL⇒ Increase dose by 25%
15-20	• If goal is 10-15 mcg/mL ⇒ no changes **or** the dose may be decreased by 250-500 mg (decrease every dose by 25%) to reduce the risk of nephrotoxicity. • If goal is 15-20 mcg/mL ⇒ No change
> 20	• Vancomycin doses should be held, and daily vancomycin levels should be repeated until the level is within the target range. A new dosing regimen should be established based on the principles outlined above.

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Adult Vancomycin Dosing and Monitoring in Renal impairment

Loading (initial) dose

- Use in seriously ill patients (e.g. requiring intensive care) and patients with complicated infections

(e.g. bacteremia, pneumonia, endocarditis, osteomyelitis, prosthetic joint infection and infection involving the central nervous system)

  - Recommended dose: 15-20 mg/kg IV (Maximum 2.5 gram)
- Based on actual body weight (ABW)
- For obese patients, initial dosing can be based on ABW and then adjusted based on serum vancomycin concentrations to achieve therapeutic levels

Maintenance dose and level monitoring

- Vancomycin Initial Dosage Regimens for Patients with Impaired Renal Function

eGFR (mL/minute per 1.73 m2)	Actual Body Weight				Timing of Trough level
	<60 kg	60 to 80 kg	81 to 100 kg	>100 kg	
>90	750 mg q8hr	1,000 mgq8hr	1,250 mg q8hr	1,500 mg q8rh	Trough 30 min before 4th dose
50 to 90	750 mg q12hr	1,000 mg q12hr	1,250 mg q12hr	1,000 mg q8hr	Trough 30 min before 4th dose
15 to 49	750 mg q24hr	1,000 mg q24hr	1,250 mg q24hr	1,500 mg q24hr	Trough 30 min before 4th dose
15[a]	750 mg	1,000 mg	1,250 mg	1,500 mg	Q24H: Trough 30 min before 4th dose Q48H: Trough 30 min before 3rd dose
<10 or AKI*, Dose by daily level	15mg/kg, then dose by level				Trough within 24H of last dose,or with morning labs, or every other day
ESRD on hemodialysis	Initial: 15-20 mg/kg (MAX 2 gm) Maintenance: According to the table below (hemodialysis)				Trough obtained prior to the third dialysis session

		following initiation of therapy
CRRT	Initial: 15-20 mg/kg (MAX 2 gm) Maintenance: 10-15 mg/kg Q24H	Trough daily q24hr before vancomycin dose
Peritonial dialysis	15-20 mg/kg IV,then dose by level. Dosing for intraperitoneal (IP) instillation intermittent (1 exchange/day): 15-30mg/kg IP initially,then dose by level supplement doses may be needed for APD	
a) Check a random vancomycin level in 24 hours after the dose. If random level is ≤20 mcg/mL, repeat the dose. If random level is >20 mcg/mL, do not redose; repeat random level in 12 hours		

eGFR : estimated glomerular filtration rate, Kg: kilogram, q8hr: every 8 hours, q12hr: every 12 hours, q24hr: every 24hr,

*AKI (based on KDIGO,RIFLE,AKIN classification):

i. SCr change by ≥0.3 mg/dl within 48H or 50% from baseline or within last 7 day
ii. CrCl change by> 25-50%
iii. urine output < 0.5 ml/kg/hr over 6 hours (oliguria)

2.Monitoring:

Vancomycin level:

- Trough serum vancomycin concentrations are the most accurate and practical method for monitoring efficacy and safety (nephrotoxicity).
- For patients with normal renal function, it takes approximately 4 doses of vancomycin to reach steady state. Trough concentration should be drawn 30 minutes before the 4th dose.
- Trough concentrations may be drawn earlier in critically ill patients, patients with unstable renal function and patients on vancomycin dosing interval more than or equal 24 hours.
- Trough concentrations must be interpreted with caution since additional doses will accumulate until steady state is reached.

Renal function:

- Monitor renal function for nephrotoxicity three time per week and more frequently when vancomycin combined with another nephrotoxic drugs (aminoglycoside, furosemide, piperacillin-sulbactam…etc)
- Vancomycin-Induced Nephrotoxicity: A minimum of two or three consecutive documented increases in serum creatinine concentrations (defined as an increase of ≥ 0.5 mg/dL or a ≥50% increase from baseline, whichever is greater) after several days of vancomycin therapy or a drop in calculated CrCl of 50% from baseline on two consecutive days in the absence of an alternative explanation.

Infusion related reaction monitoring:

- Monitor for infusion related event, including hypotension and red man syndrome.
- Rapid IV administration (<60 minutes) may increase risk of red man syndrome and may result in hypotension, flushing, erythema, urticaria, pruritus and cardiac arrest.
- CBC monitoring:
- Periodic monitoring for CBC should be done to screen for neutropenia and thrombocytopenia in patient with prolong vancomycin therapy or those whose receive concomitant drug that cause bone marrow suppression.

CBC monitoring:

- Periodic monitoring for CBC should be done to screen for neutropenia and thrombocytopenia in patient with prolong vancomycin therapy or those whose receive concomitant drug that cause bone marrow suppression.

Dosing The target trough concentration depends on the type infection :

Type of Infection	Target Trough Concentration
Uncomplicated infection (soft and skin tissue infection abscsess and cellulitis)	10 – 20 mcg/ml
Complicated infection (Endocarditis , Osteomyletis , Bactermia , Prosthetic joint infection , pneumonia and Meningitis)	15 – 20mcg/ml

3. Dose adjustment:

The Adjustment of Vancomycin doses based on the level:

Note: Always check that the dosage history and sampling time are appropriate before interpreting the result.

Trough	Recommended Adjustment
< 5	- Decrease the dosage interval to the next frequency (example: every 12 hr to every 8 hr) - Or increase the total daily dose: • If goal is 10-15 mcg/mL ⇒ Increase dose by 25% • If goal is 15-20 mcg/mL⇒ Increase dose by 50 %
5-10	• If goal is 10-15 mcg/mL ⇒ Increase dose 25% • If goal is 15-20 mcg/mL⇒ decrease the dose interval to the next frequency or Increase every dose by 50%
10-15	• If goal is 10-15 mcg/mL ⇒ No change • If goal is 15-20 mcg/mL⇒ Increase dose by 25%

15-20	• If goal is 10-15 mcg/mL ⇒ no changes or the dose may be decreased by 250-500 mg(decrease every dose by 25%) to reduce the risk of nephrotoxicity. • If goal is 15-20 mcg/mL ⇒ No change
> 20	• Vancomycin doses should be held, and daily vancomycin levels should be repeated until the level is within the target range. A new dosing regimen should be established based on the principles outlined above.

Intermittent Hemodialysis (high-flux HD) Dosing:

- Vancomycin loading dose: 15-20 mg/kg (maximum 2g) (estimated dry weight)
- A maintenance IV dose of 10 mg/kg (estimated dry weight)
- A vancomycin serum concentration should be obtained prior to the third dialysis session following initiation of therapy, and dose adjustments should be made as summarized in the thable below.
- In critically ill patients or other concern for altered pharmacokinetics (eg, residual renal function, acutely post-transplant), a pre-dialysis vancomycin concentration should be assessed prior to each dialysis session until stable dosing has been established.
- Estimated vancomycin trough concentration: Extrapolate by reducing predialysis level by 40% to account for drug removal during a 4-hour dialysis session
- Supplemental vancomycin dosing is generally required during the final hour of dialysis (to facilitate the completion of the session) or immediately following each dialysis session
- Following dose adjustment, repeat vancomycin serum concentration should be measured prior to the following dialysis session, with subsequent adjustment (if necessary) according to the table.
- Once the predialysis vancomycin concentration is within the target range, it should be checked weekly. If subsequent concentrations are outside the target range, dose adjustments should be made as a following table.

Target trough level (10-20)	
Pre-HD level	Dosing
<10 mcg/mL	Administer 1,000 mg after HD
10 to 25 mcg/mL	Administer 500 to 750 mg after HD
>25 mcg/mL	Hold vancomycin

- Redosing based on post-HD concentrations: <10 to 15 mg/L: Administer 500 to 1,000 mg

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Aminoglycosides dosing and monitoring in Adult

The traditional approach to parenteral aminoglycoside dosing in adults involves the administration of a weight-based dose divided two to three times daily in patients with normal renal function. The dose is reduced and/or dosing interval extended in patients with decreased renal function or as indicated by measured serum drug concentration(s).

Extended-interval aminoglycoside therapy (also known as once-daily aminoglycosides, single daily aminoglycoside dosing, consolidated or high-dose aminoglycoside therapy) utilizes a higher weight-based dose administered at an extended interval (every 24 hours for those with normal renal function and longer for those with renal dysfunction)

1. High-Dose Extended-Interval (Gram-negative infections)

Because of comparable efficacy and safety (for nephrotoxicity only; the meta-analyses and other studies did not demonstrate a significant difference in ototoxicity with the two regimens) with superior pharmacodynamics profiles and greater ease of administration, extended-interval (instead of traditional intermittent) aminoglycoside dosing is often preferred for patients with suspected or documented moderate to severe infections due to gram-negative aerobic bacteria and among whom this method has been clinically evaluated, including:

- Immunocompetent, no pregnant adults and children >3 months of age with
  - Urinary tract infections
  - Intraabdominal infections
  - Respiratory tract infections
  - Gynecologic infections (including pelvic inflammatory disease)
  - Soft-tissue infections
  - Bacteremia
- Women with postpartum endometritis
- Febrile neutropenia patients with malignancy (adults and children)

Exclusion Criteria:

- Renal insufficiency (CrCl <30 mL/min or rapidly declining renal function)
- Pregnancy
- Synergy for gram-positive infections
- Ascites
- Burns (>20%)

Dosing:

Intravenous administration of aminoglycosides (Gentamycin) should occur over at least 60 -120 minutes for extended interval dosing

Initial dosing:

- Usually the aminoglycoside dose is calculated by using the actual body weight
- If obese patients (total body weight (TBW) > 20% over Ideal body weight (IBW)), dosage requirement may best be estimated using an adjusted body weight
- Adjusted body weight = IBW + (0.4 [TBW– IBW])
- IBW, in kg (males) = 50 + (2.3 x inches above 60 inches)
- IBW, in kg (females) = 45 + (2.3 x inches above 60 inches)
  From cm to inch divided the length value by 2.54
  Obese: Body mass index (BMI) ≥ 30

Crcl (ml/min)	Gentmicin	Amikacin
≥ 60 ml/min	5mg/kg Q24 H (7 mg/kg if critically ill)	15 mg/kg Q24 H
40-59 ml/min	5mg/kg Q36H	15 mg/kg Q36 H
30-39 ml/min	5mg/kg Q48H	15 mg/kg Q48 H
20-29 ml/min	shift to conventioal dosing	shift to conventioal dosing
< 20 ml/min	shift to conventioal dosing	shift to conventioal dosing
Hemodialysis(check)	shift to conventioal dosing	shift to conventioal dosing
CRRT	shift to conventioal dosing	shift to conventioal dosing

1. Monitoring:

Nomogram Based Monitoring is the preferred method for aminoglycoside monitoring unless the patient developed any change in the renal function then the level must be adjusted according to Individualized Monitoring Method.

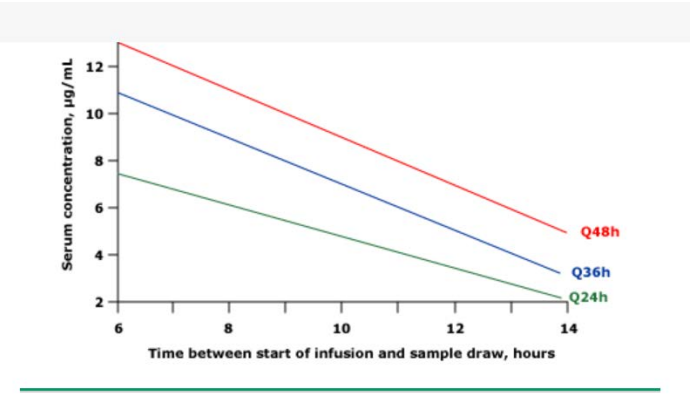
Nomogram-based monitoring:

Hartford nomogram:

- Application of the published nomogram requires that a single serum concentration be obtained 6 to 14 hours (preferably 10) after the first dose (figure 1). Results from this measurement **are then used to determine the necessary dosing interval.** Successful application of this approach has been documented

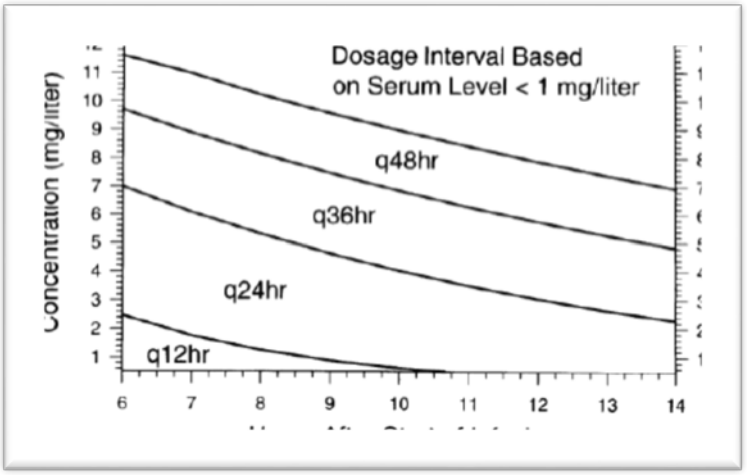
- The serum gentamicin concentration should be obtained 6 hours (or up to 14 hours) after the initial dose of 7 mg/kg and plotted on the above nomogram. The interval for drug administration of subsequent doses of 7 mg/kg (Only applicable for 7 mg/kg – plotting doses lower or higher than 7 mg/kg may under or overestimate clearance) is then determined based on the interval specified on the graph.

- Application of the nomogram for amikacin requires the measured concentration be divided by two. The new value should be plotted on the nomogram in order to obtain the appropriate dosing interval.
- Although unlikely to result in peak serum concentrations below the desired target value when doses of 7 mg/kg are employed, single-concentration serum monitoring requires assumptions that individual patients exhibit kinetic parameters comparable to other patients. Patients not conforming to usual population kinetic parameters may have suboptimal serum aminoglycoside concentrations if doses are calculated from the standard nomogram. Appropriate patient selection should significantly reduce the risk of such variability.



Urban & Craig Nomogram

- If the dose 5mg/kg use (figure 2):
- Single level drawn 8-12 hours after the first dose
- Use nomogram to confirm/modify dosage interval.
- Only applicable for 5 mg/kg
- Gentamicin 5 mg/kg/dose
- Amikacin 15 mg/kg/dose



Individualized monitoring

An alternative to the use of the nomogram is to obtain a peak serum aminoglycoside concentration (60 minutes post-infusion). Dosing adjustment based on these concentrations is generally performed with the assistance of a clinical pharmacist based on individualized patient pharmacokinetic parameters.

- Additional samples may be obtained during the course of therapy (eg, sample 6 to 12 hours post-infusion after the same dose) to verify that concentrations have not changed significantly. The disadvantage to this method is the requirement of more sophisticated analyses (usually performed by pharmacists).

- Target concentrations:
  Gentamicin: Extended-interval aminoglycoside dosing targets a peak serum concentration of approximately 15 to 20 mcg/mL in order to target approximately 10 times the MIC of the pathogen. Trough serum concentrations should be less than 1 mcg/mL (are most often undetectable) because of the extended dosing interval. The estimated drug-free interval (ie, concentration is undetectable) is less than eight hours.
  Amikacin: Higher peaks (40 to 50 mcg/mL) are generally achieved with extended interval dosing and a trough of <8 mcg/mL (often targeted at 1 to 4 mcg/mL).

Follow up trough level testing:

- Trough monitoring (30-60 minutes prior to dose) should be considered in patients demonstrating acute changes in renal function or suspicion of extended interval failure
- Maintenance random levels should be monitored at least once weekly
- If duration of therapy is anticipated to be > 2 weeks, audiometry should be considered

2. Conventional / Traditional Dosing (Gram-negative infections)

Initial dosing:

Gentamicin: initial dose: 2 mg/kg

Amikacin: initial dose: 7.5 mg/kg

Maintenance dose: depend on the renal function as following:

Crcl (ml/min)	Gentmicin/Tobramycin	Amikacin
>70 ml/min	1.7-2 mg/kg Q8 H	5 -7.5 mg/kg Q8 H
40-69 ml/min	1.7 mg/kg Q12H	5-7.5 mg/kg Q12 H
30-39 ml/min	1.7 mg/kg Q24H	5-7.5 mg/kg Q24H
20-29 ml/min	1.7 mg/kg Q24H	5-7.5 mg/kg Q24-36H
< 20 ml/min, AKI	2 mg/kg load , then dose by level	5 mg/kg load then dose by level
Hemodialysis	2 mg/kg load , then 1.5 mg/kg post HD, redose pre-dialysis or 4 hr post HD if level <1 mg/L • Target level: (mild UTI): <1 mg/L • Target level: (moderate-severe UTI) 2-3mg/L • Target level: (severe GNR infection) 3-5mg/L	5-7.5 mg/kg post HD
CRRT	1.5-2.5 mg/kg Q24-48H	10 mg/kg load , then 7.5 mg/kg Q24-48H

Monitoring:

Timing of levels		
Regimen frequency	Peak	Trough
Q8H	30 minutes after 3rd dose	30-60 minutes before 4th dose
Q12H	30 minutes after 3rd dose	30-60 minutes before 3rd dose
Q24H	30 minutes after 2nd dose	30-60 minutes before 2nd dose
Q48H	30 minutes after 2nd dose	30-60 minutes before 2nd dose
Dose by level	30 minutes after 2nd dose	Re-dose when level <1 mcg/ml
Haemodialysis	30 minutes after 2nd dose	4-hr post HD level <1 mcg/ml or pre-HD levels (see initial dosing table)
CRRT	30 minutes after 2nd dose	30-60 minutes before 3rd dose

Target levels			
Antibiotic	Indication	Target peak	Target trough
Gentmicin	Life threatening infection Serious infections Urinary tract infections	8-10 mcg/ml 6-8 mcg/ml 4-6 mcg/ml	< 1-2 mcg/ml
Amikacin	Life threatening infection Serious infections Urinary tract infections	25-30 mcg/ml 20-25 mcg/ml 15-20 mcg/ml	< 4-8 mcg/ml

Frequency of monitoring — Once the desired peak and trough serum concentrations are achieved, serum aminoglycoside concentrations should be re-evaluated throughout therapy when there are any changes in renal function. The need for repeated serum concentration monitoring once desired concentrations are achieved in patients with stable renal function is less clear. However, monitoring should be repeated at least weekly if therapy will be prolonged beyond 7 to 10 days.

3. Gram – positive Synergy Dosing: *(endocarditis)*

*Streptococci, *Streptococcus gallolyticus (bovis)*, *Streptococcus viridans* endocarditis: optional dosing 3 mg/kg q24h for CrCl > 60 mL/min. Staphylococci; Enterococcus spp (strains susceptible to PCN and gentamicin) endocarditis: optional dosing 3 mg/kg in 2 or 3 equally divided doses

CrcI (ml/min)	Synergy dosing Gentmicin/Tobramycin
> 60 ml/min	1 mg/kg Q8 H*
40-59 ml/min	1 mg/kg Q12H
30-39 ml/min	1mg/kg Q24H
20-29 ml/min	1mg/kg Q24H
< 20 ml/min, AKI	Redose when Cp <1 mg/L
Hemodialysis	1 mg/kg q48-72 H Redose for pre-HD or post-HD Cp < 1 mg/L
CRRT	1 mg/kg Q24H , then by level

Monitoring:

Timing of levels		
Regimen frequency	Peaks	Troughs
Q8H	30 minutes after 3rd dose	30-60 minutes before 4th dose
Q12H	30 minutes after 3rd dose	30-60 minutes before 3rd dose
Q24H	30 minutes after 2nd dose	30-60 minutes before 2nd dose
Q48H	30 minutes after 2nd dose	30-60 minutes before 2nd dose
Dose by level	30 minutes after 2nd dose	Redose when Cp <1 mcg/ml
Haemodialysis	30 minutes after 2nd dose	Immediately before HD , Redose for pre-HD or 4-hr post HD level: Cp <1 mg/L
CRRT	30 minutes after 2nd dose	30-60 minutes before 3rd dose

Target level		
Antibiotic	Target peak	Target trough
Gentmicin/Tobramycin	3-4 mcg/mL	< 1mcg/mL

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