IREDELL HEALTH SYSTEM

Adult Pharmacokinetic Dosing Protocol	
Approved by: Laura Rollings, PharmD, BCPS, BCGP Dr. Robert Aryeetey, Infectious Disease	Last Revised/Reviewed Date: 01/2021
Antimicrobial Stewardship Committee P&T Committee	Date: 03/2021 Date: 03/2021

PURPOSE

To assure consistent and optimal dosing and monitoring of vancomycin and aminoglycosides, clinical staff pharmacists will provide a pharmacokinetic (PK) service for adults.

POLICY

The Adult Pharmacokinetic Dosing Protocol will be initiated when the physician orders "Vancomycin Protocol", "Vancomycin-Pharmacy to Dose", or an equivalent order. It will also apply to aminoglycosides when ordered in the same manner. This order will initiate the ordering and monitoring of vancomycin and aminoglycoside therapy for adult patients by pharmacists according to the following protocol. ICS (Infusion Care Services) patients will be included in this protocol. Pre-admission emergency department patients and those receiving vancomycin or aminoglycosides for surgical prophylaxis will not be included in this protocol.

PROCEDURES

I. Processing New Orders

1. A "Vancomycin/Aminoglycoside-Pharmacy to Dose" order will be linked to the respective order for patients starting vancomycin or an aminoglycoside for which therapy is planned to continue.
    a. The verifying pharmacist will review and verify the order and initiate an appropriate initial dosing regimen
        i. Loading doses will be reviewed and provided promptly
        ii. Orders for maintenance doses and monitoring will be provided by a pharmacist prior to the next dose due
    b. Any order stating "pharmacy to dose" or "consult pharmacy" in regards to vancomycin/aminoglycoside orders will be interpreted as full dosing privileges as stated within this protocol.
    c. Providers do have the option of opting out of the pharmacy to dose protocol by not ordering it as so, discontinuing the order or notifying the pharmacist who will then discontinue the order.

II. Patient Assessment/Data Collection/Monitoring

1. Upon receiving a new "Pharmacy to Dose" order, the pharmacist will review the appropriateness of the indication and dose the antibiotic based on the below information:
    a. Clinical Indication
    b. Age
    c. Sex
    d. Height/Weight
    e. Renal function
    f. Estimated PK parameters
2. Routine monitoring will include the evaluation of clinical status, interpretation of relevant labs, drug concentrations, changes in renal function or fluid status, microbiology results, concurrent antimicrobial therapy as well as length of therapy. This information will all be recorded within a pharmacy-monitoring program in a timely manner.
3. The pharmacist will be expected to provide dosing and monitoring services until therapy is completed, discontinued or the patient is discharged.

III. Pharmacist Ordering

1. Doses
    a. Upon selecting a dosing regimen, the pharmacist will enter applicable orders.

b. All orders in response to "Pharmacy to Dose" will be entered or discontinued "per protocol-no cosign required."

2. Serum Drug Concentrations
    a. The pharmacist will order serum drug concentrations for the drug as necessary "per protocol-no cosign required."
3. Labs
    a. The pharmacist will ensure that relevant labs (SCr) are ordered, collected, resulted and recorded within he pharmacy-monitoring program. The pharmacist will ensure the relevant labs are utilized in the evaluation of appropriate dosing. Any labs ordered will be entered as "per protocol-no cosign required." The pharmacist will follow up on any labs not resulted in a timely manner. If not resulted by end of shift, the pharmacist will complete a handoff to the next shift pharmacist for follow-up.

IV. Documentation

1. Pharmacist will document within the pharmacy-monitoring program daily and with each evaluated serum creatinine, resulted concentration and/or dose change.
2. Pharmacist will document a progress note within the patient's electronic medical record (EMR) upon each resulted concentration and/or dose change.

V. Competency Standard

A pharmacy-based PK competency is required upon hire of all pharmacists participating in the PK protocol. Progress will be assessed annually as part of the annual performance review.

PROCEDURE FOR VANCOMYCIN DOSING AND MONITORING

I. Estimate Patient's Creatinine Clearance (CrCl)

$$\text{CrCl mL/min} = \frac{(140 - \text{age}) \times \text{IBW*}\ (\text{kg})}{72 \times \text{SCr}} \quad (\times 0.85 \text{ if female})$$

**Ideal Body Weight (IBW) – see Aminoglycoside section below.*

II. Choose the Appropriate Loading and Maintenance Doses Based on CrCl

Vancomycin Goal Trough Concentrations Based on Indication	
Indication	**Goal Trough Concentration (mcg/mL)**
Skin and soft tissue infections, urinary tract infection, febrile neutropenia	10 - 15
Bacteremia, endocarditis, meningitis, pneumonia, osteomyelitis, septic arthritis, pacemaker pocket infections, sternal wound infections, VAD infections, sepsis, severe skin and skin structure infection (necrotic, involving tissue)	15 - 20
Consider for meningitis	> 20

Empiric Vancomycin Maintenance Dose and Frequency							
Goal Trough Concentration	**Loading Dose**	**Maintenance Dose (Round to nearest 250 mg; Maximum dose 2000mg)**	**Dosing Interval Based on Estimated CrCl (mL/min)**				
			> 70	**50 – 69**	**35 – 49**	**15-34**	**< 15 or Dialysis**
10 – 15 mcg/mL	None	15 mg/kg	q12h	q24h	q24h	Based on Concentration	
15 – 20 mcg/mL	20 mg/kg	15 mg/kg	q8h	q12h	q24h	Based on Concentration	

III. Therapeutic Drug Monitoring

A. Trough Concentrations

- Only necessary if receiving vancomycin beyond 72 hours
- Recommended for those with unstable renal function, those receiving aggressive dosing, those at high risk of nephrotoxicity, and in those receiving prolonged courses of therapy (greater than 3-5 days)
- Obtain when the concentrations is at steady state (with the 4th or 5th dose)
- For dosing intervals ≥ 48 hours, obtain trough prior to the 3rd dose
- Concentrations should be obtained no earlier than 30 minutes prior to dose
- Reorder new trough concentration after each change in dosage to ensure new regimen is appropriate
- Any true trough concentration > 30mcg/mL should result in holding therapy until concentration has fallen into therapeutic range
- Once stable on a dosing regimen, monitor trough every 5 to 7 days
- If renal function is unstable consider checking trough every 3 days

- Troughs should be checked daily for patients receiving q8h dosing

B. Peak Concentrations

- Unnecessary in the majority of patients

C. Random Concentrations

- May be necessary in the following situations: acute renal failure or steadily rising SCr, dosing the antibiotic by concentration, if patient is experiencing significant fluid status changes, and critically ill patients, and patients receiving vancomycin prior to admission or transfer in (e.g. outpatient parenteral antibiotic therapy, hemodialysis center or outside facility).
    - ❖ Random concentrations should generally be ordered and drawn with AM labs. However situations may warrant specifically timed concentrations (e.g. 12 or 24 hours after a dose is administered)
- If dosing by concentration, re-dose when concentration is ≤ 12-20 mcg/mL
    - ❖ Typical doses for re-dosing are 15-20mg/kg using total body weight (TBW)

D. Other Monitoring

- Serum Creatinine (SCr) will be monitored at the initiation of therapy, and routinely during treatment. Typically, daily SCr is monitored for patients receiving treatment for confirmed infection until steady state is achieved and weekly thereafter. SCr will be monitored daily for the first 7 days of therapy and until steady state is achieved. Following the initial 7 days, if SCr is stable, it will be monitored when trough levels are obtained. Pharmacists may order labs more frequently, if needed.
    - ❖ For ICS patients receiving vancomycin, obtain a SCr at baseline and with each vancomycin concentration.
    - ❖ In patients receiving dialysis, only monitor SCr with concentrations. Daily SCr is unnecessary since these patients have little to no renal function
- Urine output will be monitored by pharmacists when data is available in the medical record.

E. Provider Notification

- Pharmacists will notify provider if SCr increases by 0.5 mg/dL or more from baseline.

IV. Vancomycin Dose Adjustments

A. Before adjusting doses, verify that the concentration was drawn at the appropriate time and that the previous dose was not given late or that recent doses have not been missed.

B. Refer to **Appendix A** for vancomycin adjustment calculations

V. Special Populations

A. Patients in whom SCr does not reflect vancomycin clearance. These cases MAY warrant dosing by concentration and/or aggressive monitoring

- Amputees
- Low muscle mass (cerebral palsy, muscular dystrophy, ALS, para/quadriplegics, elderly or immobile)
- Severe CHF or Cardiogenic shock
- Critically ill/septic shock
- Cirrhosis/ascites
- Acutely changing renal function

B. Patients with risk factors for renal dysfunction

- Diabetes mellitus
- Age > 65 years
- Nephrotoxic medication administration (diuretics, aminoglycosides, etc.)
- Recent or current use of piperacillin-tazobactam
- Recent or current use of contrast agents
- History of chronic kidney disease or solitary kidney

C. Patient's with altered volume of distribution

- Burn patients
- Critically ill/septic shock
- CHF/fluid overload

- Cirrhosis
- ESRD
- Obesity – BMI >30
- Fluid shifts

D. Intermittent Hemodialysis (IHD)

- Upon receiving an order for Vancomycin – Pharmacy to Dose, pharmacist will place an initial loading dose pf 20 mg/kg.
- Following a loading dose, pharmacy will input an initial maintenance dose of 10 mg/kg to be administered with dialysis treatments and adjusted thereafter with each dialysis treatment. Maintenance doses should be administered during each dialysis treatment in the last 1 – 2 hours of the session.
- Troughs should be obtained immediately prior to dialysis sessions. If the patient is being dialyzed intermittently and dialysis treatments are not performed for > 48 hours, a random level may be required between treatments to ensure adequate serum concentrations.
- Dose adjustments should occur as outlines below with each trough level obtained:

Pre-dialysis vancomycin concentration (mcg/mL)	**Dosage adjustment**
< 15	↑ dose by 250 – 500 mg
15 – 25	No change in current therapy
26 – 30	↓ dose by 250 – 500 mg
> 30	HOLD vancomycin dose

*The following recommendations assume the patient is receiving high-flux IHD 3x/weekly.

- Note: Approximately 25 – 30 % of pre-dialysis is removed by hemodialysis.

E. Peritoneal Dialysis

- Upon receiving an order for Vancomycin – Pharmacy to Dose, pharmacist will place an initial loading dose of *intravenous* vancomycin 20 mg/kg (TBW) x1.
- Intermittent intravenous vancomycin doses should be 15 mg/kg x1 should be given based on goal trough concentrations.
- Random concentrations should be obtained approximately 48 hours after a dose and with AM labs, is possible. Repeat doses should be administered once concentrations are < 20 mcg/mL (generally HS before cycle)
- Intra-peritoneal vancomycin is not recommended in patients with IV access.
    - For peritonitis in a PD patient only, intraperitoneal administration is the preferred route. Nephrologists are responsible for managing peritonitis in a PD patient.

AMINOGLYCOSIDES – EXTENDED INTERVAL DOSING AND MONITORING

Extended interval aminoglycoside dosing will be initiated for all patients when the physician writes for "Tobramycin/Gentamicin/Amikacin-Pharmacy to Dose", except for those patients meeting any of the exclusion criteria listed below.

Rationale:

- Aminoglycosides display concentration-dependent bactericidal action. Therefore, higher doses and serum concentrations result in more rapid bacterial killing.
- Aminoglycosides also exhibit a long post-antibiotic effect, exhibiting persistent bacterial suppression even after the serum levels falls below the minimum inhibitory concentration.
- This may potentially reduce renal and auditory accumulation of the aminoglycoside, reducing the risk of toxicity.

Exclusion Criteria:

Chronic renal insufficiency (CrCl < 30 mL/min)
Acute renal failure (increase in SCr 30% above baseline)
Treatment of Gram (+) infections/synergy (endocarditis, meningitis, MSSA cellulitis)
ESRD on any form of renal replacement therapy
Pregnancy
Severe CHF patients/Cardiogenic shock
Liver failure with ascites
Burns covering > 20% of the total BSA
Surgical prophylaxis

Procedure:

I. Determine Patient's Dosing Weight (DW)

a. Non-Obese Patients:
Use total body weight (TBW). Non-obese is defined as a TBW < 120% over ideal body weight (IBW)

IBW (males) = 50 + (2.3 x height in inches > 60 inches)
IBW (females) = 45 + (2.3 x height in inches > 60 inches)

b. Obese Patients:
Use adjusted body weight (ABW) in obese patients. Obese is defined as a TBW > 120% of IBW

ABW (kg) = IBW + 0.4 (TBW - IBW)

II. Determine Patient's Dose

Gentamicin /Tobramycin: 7 mg/kg x DW (10 mg/kg for cystic fibrosis)
Amikacin: 15 mg/kg x DW

III. Estimate Patient's Creatinine Clearance (CrCl)

$$\text{CrCl mL/min} = \frac{(140 - \text{age}) \times \text{IBW (kg)}}{72 \times \text{SCr}} \quad (\times 0.85 \text{ if female})$$

IV. Determine Patient's Dosing Interval Based on CrCl

CrCl (mL/min)	Dosing Interval
> 60	Q24h
40 – 59	Q36h OR use conventional dosing
20 – 39	Q48h OR use conventional dosing
< 20	Not eligible, use conventional dosing

V. Therapeutic Drug Monitoring

A. Random Concentrations

- Obtain 8-12 hours after the start of the FIRST dose
- Plot random concentration on the Hartford Nomogram below to determine the need for dosing interval adjustments (for amikacin, divide level by two and then plot on nomogram)
    - If random concentration falls within an interval area, that is the respective interval
    - If random concentration falls on a line, extend the interval to a longer dosing interval
    - If random concentration falls above the 48 hour line, switch to traditional dosing

B. Trough Concentrations

- Once dosing interval has been determined using the nomogram, repeat concentrations will be monitored in the form of TROUGHS
- Concentrations should be obtained no earlier than 30 minutes prior to the next dose
- Goal Trough Concentrations
    - Gentamicin/Tobramycin <1 mcg/mL
    - Amikacin <4 mcg/mL
- Extend dosing interval if trough is above goal or see Appendix A for PK based adjustments
- Once stable on a dosing regimen, monitor trough every 5 to 7 days
- If renal function is unstable consider checking trough every 3 days

C. Peak Concentrations

- NOT routinely monitored for extended interval dosing

D. Other Monitoring

- SCr will be monitored at the initiation of therapy, and routinely during treatment. Typically, daily SCr is monitored for patients receiving treatment for confirmed infection until steady state is achieved and weekly thereafter. SCr will be monitored daily for the first 7 days of therapy and until steady state is achieved. Following the initial 7 days, if SCr is stable, it will be monitored when trough levels are obtained. Pharmacists may order labs more frequently, if needed.
    - ❖ <u>For ICS patients receiving aminoglycosides, obtain a SCr at baseline and with each aminoglycoside concentration.</u>
    - ❖ In patients <u>receiving dialysis,</u> only monitor SCr with concentrations. Daily SCr is unnecessary since these patients have little to no renal function
- Urine output will be monitored by pharmacists when data is available in the medical record.

E. Provider Notification

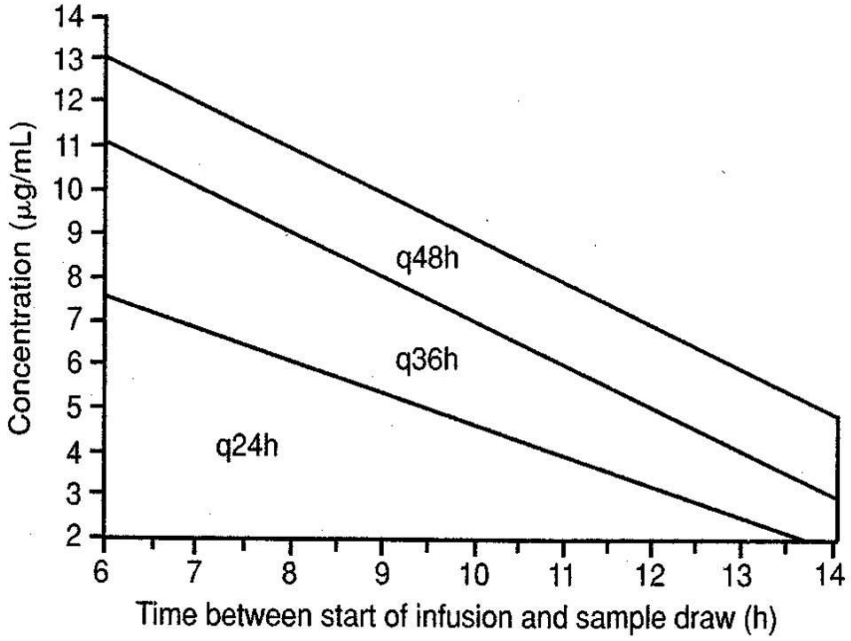
- Pharmacists will notify provider if SCr increases by 0.5 mg/dL or more from baseline.

VI. Aminoglycoside Dosing Adjustments

A. Before adjusting doses, verify that the concentration was drawn at the appropriate time and that the previous dose was not given late or that recent doses have not been missed.

B. Refer to **Appendix A** for aminoglycoside adjustment calculations

Hartford Nomogram (Extended Interval Therapy)



- Gentamicin/Tobramycin (7mg/kg/dose): plot on graph
    - If using 5 mg/kg/dose, the resulting level must be multiplied by a factor to equal 7 mg divided by the dose used. Example: If a patient is receiving 5 mg/kg/day and the 10 hour post-dose level was 2 mcg/mL, multiply the level by 1.4 (7/5) to get a level of 2.8 mcg/mL. This adjusted level is what is to be plotted on the Hartford Nomogram.
- Amikacin (15mg/kg/dose): divide concentration in half, then plot on graph
- Plotting doses lower or higher than the above may over or underestimate clearance.

AMINOGLYCOSIDES – TRADITIONAL DOSING AND MONITORING

When an order is written for "Tobramycin/Gentamicin/Amikacin-Pharmacy to Dose", the pharmacist will determine whether to use the traditional or extended interval protocols. The traditional dosing protocol will be used for those patients who are excluded from the extended interval dosing protocol.

Procedure:

I. Determine Patient's Dosing Weight (DW)

a. Non-Obese Patients:
Use total body weight (TBW). Non-obese is defined as a TBW < 120% over ideal body weight (IBW)

IBW (males) = 50 + (2.3 x height in inches > 60 inches)
IBW (females) = 45 + (2.3 x height in inches > 60 inches)

b. Obese Patients:
Use adjusted body weight (ABW) in obese patients. Obese is defined as a TBW > 120% of IBW

$$ABW\ (kg) = IBW + 0.4\ (TBW - IBW)$$

II. Estimate Patient's Creatinine Clearance (CrCl)

$$CrCl\ mL/min = \frac{(140 - age) \times IBW\ (kg)}{72 \times SCr} \quad (\times 0.85 \text{ if female})$$

III. Determine Desired Concentration Based on Indication

Indication/Site of Infection	Desired Concentrations (mcg/mL)			
	Gentamicin/Tobramycin		Amikacin	
	Peak	Trough	Peak	Trough
Uncomplicated UTI, synergy	3 – 5 mcg/mL	< 1 mcg/mL	15 – 20 mcg/mL	< 4 mcg/mL
Moderate gram (-) infections, soft tissue infections, open fracture prophylaxis, pyelonephritis	6 – 8 mcg/mL	< 1 mcg/mL	20 – 35 mcg/mL	< 4 mcg/mL
Gram (-) sepsis, pneumonia, life threatening infections	8 – 10 mcg/mL	< 2 mcg/mL	30 – 35 mcg/mL	< 8 mcg/mL

IV. Select Appropriate Loading and Maintenance Doses Based on Estimated CrCl

Drug	Goal Peak Concentration (mcg/mL)	Loading Dose*	Maintenance Dose	Dosing Interval Based on Estimated CrCl (mL/min)			
			CrCl > 80 mL/min	65 – 80	35 – 65	20 – 35	< 20 or dialysis
Gentamicin or Tobramycin	3 – 5	1 mg/kg	1 mg/kg q8h	q12h	q24h	q48h	Based on Concentration
	6 – 8	2 mg/kg	1.5 mg/kg q8h				
	8 – 10	2 – 3 mg/kg	2- 2.5 mg/kg q8h				
Amikacin	15 – 20	-	4 mg/kg q8h	q12h	q24h	q48h	Based on Concentration
	20 – 35	-	6 mg/kg q8h				
	30 – 35	-	10 mg/kg q8h				

**Loading dose only needed in life-threatening infections or in dialysis patient to achieve steady state levels more rapidly.*

V. Therapeutic Drug Monitoring

- **Trough Concentrations**
  - Obtain when the concentrations is at steady state (with the 4th or 5th dose)
  - Concentrations should be obtained no earlier than 30 minutes prior to dose
  - For dosing intervals ≥ 48 hours, obtain trough prior to the 3rd dose or within 72 hours
  - Reorder new trough concentration after each change in dosage
  - Once stable on a dosing regimen, monitor trough every 5 to 7 days
  - If renal function is unstable consider checking trough every 3 days
- **Peak Concentrations**
  - Obtain when the concentrations is at steady state (with the 4th or 5th dose)
  - Concentrations should be obtained 30 minutes after the end of the infusion
  - Reorder new peak concentration after each change in dosage
  - Once stable on a dosing regimen, monitor peak every 5 to 7 days
  - If renal function is unstable consider checking peak every 3 days
- **Random Concentrations**
  - May be necessary in the following situations: acute renal failure or steadily rising SCr, dosing the antibiotic by concentration, if patient is experiencing significant fluid status changes, and critically ill patients.
    - ❖ Random concentrations should generally be ordered and drawn with AM labs. However situations may warrant specifically timed concentrations (e.g. 12 or 24 hours after a dose is administered)
- **Other Monitoring**
  - Serum Creatinine (SCr) will be monitored at the initiation of therapy, and routinely during treatment. Typically, daily SCr is monitored for patients receiving treatment for confirmed infection until steady state is achieved and weekly thereafter. SCr will be monitored daily for the first 7 days of therapy and until steady state is achieved. Following the initial 7 days, if SCr is stable, it will be monitored when trough levels are obtained. Pharmacists may order labs more frequently, if needed.
    - ❖ <u>For ICS patients receiving aminoglycosides, obtain a SCr at baseline and with each aminoglycoside concentration.</u>
    - ❖ In patients <u>receiving dialysis</u>, only monitor SCr with concentrations. Daily SCr is unnecessary since these patients have little to no renal function.
  - Urine output will be monitored by pharmacists when data is available in the medical record.

E. Provider Notification

- Pharmacists will notify provider if SCr increases by 0.5 mg/dL or more from baseline.

VI. Special Populations

A. Patients in whom SCr does not reflect vancomycin clearance. These cases MAY warrant dosing by concentration and/or aggressive monitoring

- Amputees
- Low muscle mass (cerebral palsy, muscular dystrophy, ALS, para/quadriplegics, elderly or immobile)
- Severe CHF or Cardiogenic shock
- Critically ill/septic shock
- Cirrhosis/ascites
- Acutely changing renal function

B. Patients with risk factors for renal dysfunction

- Diabetes mellitus
- Age > 65 years
- Nephrotoxic medication administration (diuretics, aminoglycosides, etc.)
- Recent or current use of piperacillin-tazobactam
- Recent or current use of contrast agents
- History of chronic kidney disease or solitary kidney

C. Patient's with altered volume of distribution

- Burn patients
- Critically ill/septic shock
- CHF/fluid overload
- Cirrhosis
- ESRD
- Obesity – BMI >30
- Fluid shifts

D. Intensive Care Unit Patient
- These patients have dynamic changes in fluid status and renal function and often standing dosing regimens cannot be used.
- Dose based on the desired peak concentration.
  Dose= desired peak X Vd (0.3 L/kg X dosing weight above)
- Perform intense monitoring- often peak and random level at 12 hours (8 hours if excellent clearance expected) with first dose is recommended to determine true Vd and elimination rate. This will allow calculation of the dosing interval.

E. Intermittent Hemodialysis (IHD)
- Upon receiving an order for Gentamicin/Tobramycin/Amikacin – Pharmacy to Dose, pharmacist will place an initial loading dose based on indication (see TABLE 1).
- Maintenance dose, as detailed in TABLE 1, shall be administered post-dialysis. Pharmacy will place appropriate with dialysis treatments.
- Concentrations shall be obtained as detailed in TABLE 2.
- Note, Approximately 25 -30 % of pre-dialysis concentration is removed by hemodialysis.

F. Peritoneal Dialysis
- Traditional dosing of Aminoglycosides for peritoneal dialysis patients is contraindicated.
- Intra-peritoneal aminoglycosides are not recommended in patients with IV access.
  - For peritonitis in a PD patient only, intraperitoneal administration is the preferred route. Nephrologists are responsible for managing peritonitis in a PD patient.

TABLE 1:

Drug	Goal Peak Concentration (mcg/mL)	Load Dose	Maintenance Dose
Gentamicin or Tobramycin	**3 – 5**	**1 mg/kg x 1**	• Traditional: 1 .5 mg/kg post-HD (moderate infection) OR dose by concentration (Severe GNR infection) • Gram-Positive Synergy: 1 mg/kg post-HD
	6 – 8	**2 mg/kg x 1**	
	8 – 10	**2 – 3 mg/kg x 1**	
Amikacin	**15 – 20**	**4 mg/kg x 1**	• 5 – 7.5 mg/kg post-HD (adjust by concentration if needed for GNR infection)
	20 – 35	**6 mg/kg x 1**	
	30 - 35	**10 mg/kg x 1**	

TABLE 2:

Traditional and Gram-Positive Synergy Timing of Concentrations	
	Hemodialysis
PEAK	2 hours after 2nd dose • Target peak C_p post HD ~ 8mg/L 96 – 10 mg/L); ~3 – 5 mg/L (synergy)
TROUGH	Immediately before HD; re-dose for pre-HD: • Cp < 1 mg/L (mild UTI and synergy) • Cp < 2 – 3 mg/L (moderate – severe UTI) • Cp < 3 – 5 mg/L (severe GNR infection)

INITIAL EFFECTIVE DATE: 01/2018
DATES REVISIONS EFFECTIVE: 07/2018, 04/2019, 11/2019, 03/2021
DATES REVIEWED (no changes):

APPENDIX A: PHARMACOKINETIC EQUATIONS

Parameter	Vancomycin	Gentamicin/Tobramycin	Amikacin
Ke	(0.00083 x CrCl) + 0.0044	(0.0026 x CrCl) + 0.014	(0.0022 x CrCl) + 0.01
Vd	0.7 L/kg x TBW (kg)	0.25 – 0.3 L/kg x TBW* 0.3 L/kg x TBW* (ICU) 0.3 L/kg x TBW* + L of fluid overload	0.25 – 0.3 L/kg x TBW* 0.3 L/kg x TBW* (ICU) 0.3 L/kg TBW* + L of fluid overload
$t_{1/2}$	0.693/Ke	0.693/Ke	0.693/Ke
Dosing Frequency	Refer to chart in guidelines	$\frac{\ln(\text{desired pk/desired tr})}{ke} + t'$	$\frac{\ln(\text{desired pk/desired tr})}{ke} + t'$
Dose	Based on 15-20mg/kg	$\frac{\text{Desired Peak} \cdot Vd \cdot ke \cdot t' \cdot 1-e^{-ke\tau}}{1-e^{-ket'}}$	$\frac{\text{Desired Peak} \cdot Vd \cdot ke \cdot t' \cdot 1-e^{-ke\tau}}{1-e^{-ket'}}$
Prospective Peak (Single Dose)	Dose (mg) / Vd	Dose (mg) / Vd	Dose (mg) / Vd
Prospective Peak	$\frac{Dose}{Vd \cdot ke \cdot t'} \times \frac{1-e^{-ket'}}{1-e^{-ke\tau}} \times e^{-keT}$	$\frac{Dose}{Vd \cdot ke \cdot t'} \times \frac{1-e^{-ket'}}{1-e^{-ke\tau}} \times e^{-keT}$	$\frac{Dose}{Vd \cdot ke \cdot t'} \times \frac{1-e^{-ket'}}{1-e^{-ke\tau}} \times e^{-keT}$
Prospective Trough Decay Equation	Peak x $e^{-ke\Delta t}$ $C_1 = C_2 \times e^{-ke\Delta t}$	Peak x $e^{-ke\Delta t}$ $C_1 = C_2 \times e^{-ke\Delta t}$	Peak x $e^{-ke\Delta t}$ $C_1 = C_2 \times e^{-ke\Delta t}$

Patient Specific Equations for Aminoglycosides		
Parameter	**Gentamicin/Tobramycin**	**Amikacin**
Ke	$\frac{Ln(Cpeak/Ctrough)}{\Delta t}$ or $\frac{lnCpeak - lnCtrough}{\Delta t}$	$\frac{Ln(Cpeak/Ctrough)}{\Delta t}$ or $\frac{lnCpeak - lnCtrough}{\Delta t}$
True Peak	Cmax / e^{-keT}	Cmax / e^{-keT}
True Trough	Cmin x e^{-ket}	Cmin x e^{-ket}
Vd (L)	$\frac{Dose}{Peak \cdot ke \cdot t'} \times \frac{1-e^{-ket'}}{1-e^{-ke\tau}} \times e^{-keT}$	$\frac{Dose}{Peak \cdot ke \cdot t'} \times \frac{1-e^{-ket'}}{1-e^{-ke\tau}} \times e^{-keT}$
General Equations		
CrCl (mL/min)	$\frac{(140 - age) \times IBW\ (kg)}{72 \times SCr}$ (x 0.85 if female)	
Ideal Body Weight	Males = 50 + (2.3 x height in inches > 60 inches) Females = 45 + (2.3 x height in inches > 60 inches)	
Adjusted Body Weight	ABW (kg) = IBW + 0.4 (TBW - IBW)	
*Use TBW unless the patient's TBW is > 120% of IBW; If TBW is > 120% of IBW, use ABW (equations above)		

Ke = Elimination constant
$t_{1/2}$ = Half-life
T = Time lapsed from end of infusion and time peak drawn in hours
t = Time between trough level and end of interval in hours
Δt = Time between two measured concentrations or change in time
Vd = Volume of distribution
t' = Infusion time in hours
τ = Dosing interval