CONSULT RESPONSIBILITIES:
- Pharmacy will initiate and modify vancomycin for ALL patients admitted to PAMC upon receipt of the initial vancomycin order unless otherwise specified in the vancomycin order or if ordered by an Infectious Disease physician without a pharmacy to dose vancomycin consult.
- The Infectious Diseases Clinical Pharmacy Specialist will evaluate all vancomycin regimens with doses >4 gm/day for appropriateness and opportunity for pharmacokinetic/pharmacodynamic dose optimization.

LABORATORY TESTS:
- The following laboratory tests may be ordered by a pharmacist for ANY patient currently receiving vancomycin at PAMC.
  - BMP (Or individual BUN/SCr)
    - NOTE: SCr MUST be obtained and assessed prior to placement of an order for ongoing vancomycin administration.
    - First doses may be given prior to obtaining a SCr
  - Vancomycin levels (random, post-infusion, and trough)
  - Vancomycin Etest if MRSA isolated from blood or CSF

ADULT LOADING DOSE RECOMMENDATIONS:
- Loading doses will ONLY be given to individuals with the following indications: bacteremia, endocarditis, meningitis, and hospital acquired pneumonia caused by methicillin resistant Staphylococcus Aureus, severe sepsis, or as specified by prescriber.
  - See definition of severe sepsis under loading dose section below
- Recommended Loading Dose:
  - Patient’s ABW <120% of IBW:
    - 25-30 mg/kg x 1 dose based on actual body weight.
    - Max 3 grams.
  - Patient’s ABW >120% IBW:
    - 25-30 mg/kg x 1 dose based on adjusted body weight.
    - Max 3 grams.
  - Patients > 150 Kg:
    - See serial kinetic section below

ADULT MAINTENANCE DOSE RECOMMENDATIONS:
- The pharmacokinetic calculator approved for use at PAMC as the primary calculator for dosing is the Excel® PAMC Vancomycin Pharmacokinetic Calculator available on the pharmacy intranet.
- Maintenance Dose Recommendations:
  - Patient’s ABW <120% of IBW:
    - 15-20 mg/kg/dose based on actual body weight.
    - Max 2 grams
  - Patient’s ABW ≥120% of IBW:
    - 15-20 mg/kg/dose based on adjusted body weight as calculated above.
    - Max 2 grams
  - Patients > 150 Kg:
    - See serial kinetic section below

ADULT INTERVAL RECOMMENDATIONS:
- Normal renal function (CrCl > 90 ml/min): q8-12hrs
- Mild renal impairment (CrCl 50-90 ml/min) or age >60 y/o: q12-24hrs
- Moderate renal impairment (CrCl 20-49 ml/min): q24hrs
- Severe renal impairment (non-HD): Interval determined by serum vancomycin levels
  - May be unable to schedule a “regular” maintenance interval (i.e. “dose by levels” for duration of therapy).

ADULT DOSE ADJUSTMENT:
- See procedure outlined below in “Adjustment of Vancomycin Dosing Based on Trough Levels” section

- **Vancomycin Dosing in Special Adult Populations:**
  - See below section “Vancomycin Dosing in Special (ADULT) Patient Populations” for information regarding vancomycin dosing in:
    - Hemodialysis
    - CRRT
    - Pregnancy
    - Patients >150 Kg
    - AUC:MIC dosing

- **Neonatal Initial Vancomycin Dosing:**
  - **Initial Dosing:**
    - 10-15 mg/kg/dose (all ages with normal renal function) for all indications
    - Interval is determined by age related renal function (see table below):

<table>
<thead>
<tr>
<th>Postmenstrual Age (wks)</th>
<th>Postnatal Age (days)</th>
<th>Interval (hrs)</th>
</tr>
</thead>
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<td>8</td>
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<tr>
<td>&gt;45</td>
<td>All</td>
<td>6</td>
</tr>
</tbody>
</table>

- **Pediatric Initial Dosing Recommendations:**
  - Age: 1 month (and post-menstrual age >44 weeks) – 12 years:
    - 15-20 mg/kg/dose IV q6hrs (60-80 mg/kg/day)
  - Age: 12 years – 18 years:
    - 15-20 mg/kg/dose IVq6-8hrs (60-80 mg/kg/day)
  - Interval in renally impaired pediatric patients determined on case by case basis based on SCr and UOP.

- **Goal Trough Recommendations:**
  - **Adults:**
    - All indications in adults will be maintained > 10 mcg/mL in order to prevent emergence of resistance and MIC creep.
      - NOTE: Exception may be AUC:MIC dosing strategies as outlined below under “Vancomycin Dosing in Special Patient Populations”.
    - **Trough goal = 15-20 mcg/mL:** Staphylococcus aureus bacteremia, endocarditis, meningitis, osteomyelitis/septic arthritis, necrotizing fasciitis, and hospital-acquired pneumonia caused by MRSA.
    - **Trough goal = 10-15 mcg/mL:** All other indications/organisms.
    - AUC:MIC pharmacokinetic dosing may be recommended as outlined in the below “AUC:MIC Pharmacokinetic” section.
  - **Neonates:**
    - **Trough goal = 15-20 mcg/mL:** Staphylococcus aureus bacteremia, endocarditis, meningitis, osteomyelitis/septic arthritis, necrotizing fasciitis, and hospital-acquired pneumonia caused by MRSA.
    - **Trough goal = 10-15 mcg/mL:** All other indications/organisms.
    - There is insufficient evidence in neonates to suggest efficacy with utilization of lower trough goals (as in pediatrics) or AUC:MIC dosing.
  - **Pediatric Patients:**
    - **Trough goal = 10-15 for all indications/organisms**
      - Higher trough goals (15-20 mcg/mL) may be considered for patients with Staphylococcal meningitis or VP shunt infection; however, vancomycin serum levels may not correlate well with CSF levels given poor penetration. Little
evidence exists regarding use of serum vancomycin levels as predictors of success in this infection type. Infectious Diseases and Neurosurgery should be consulted and intraventricular vancomycin should be considered.

- AUC:MIC pharmacokinetic dosing may be recommended as outlined in the below “AUC:MIC Pharmacokinetic” section.
  - During therapy there may be an indication for a trough goal to be modified. The dosing pharmacist will contact the provider prior to adjusting goal vancomycin trough should this circumstance arise.

- **Vancomycin Trough Frequency/Timing (Adults, NEONATES, AND Pediatrics):**
  - Timing in Relation to Dose:
    - Draw trough within 30 minutes prior to the next dose.
  - Initial Troughs:
    - Obtain trough when vancomycin steady state is achieved (i.e. just prior to 4th dose of vancomycin (including loading dose)).
    - In some patients vancomycin troughs may not be needed. If patient’s meet ALL of the below criteria they may be eligible to NOT have trough levels drawn.
      - Anticipate duration of therapy <5 days
      - No vancomycin induced nephrotoxicity risk factors
        - See “Nephrotoxicity” section below
      - Indication warranting goal trough target of 10-15 mcg/mL
  - Ongoing:
    - Obtain trough levels just prior to 4th dose (i.e. when concentration steady state has been reached) of new regimens as appropriate when previous regimen is changed in response to subtherapeutic or supratherapeutic vancomycin level.
    - Troughs should be drawn WEEKLY at minimum throughout prolonged therapy in hemodynamically stable patients.
    - Troughs need to be drawn more often (every 3-5 days at minimum) in:
      - Hemodynamically unstable patients
      - Those with rapidly changing/unstable renal function
        - Patient with worsening renal function may need to be evaluated for likelihood of development of vancomycin induced nephrotoxicity.
        - Ongoing use/addition of concurrent nephrotoxin (i.e. NSAIDs, loop diuretic, aminoglycoside, piperacillin/tazobactam, or amphotericin B).

- **Lab Frequency/Timing for Monitoring:**
  - Serum Creatinine (SCr) should be obtained:
    - At baseline
      - NOTE: Baseline BUN/SCr MUST be obtained prior to scheduling of ongoing vancomycin regimen (i.e. must be obtained at minimum prior to 2nd dose).
    - Ongoing:
      - Weekly at minimum in patients on vancomycin
      - Daily in patients with unstable renal function
      - At least every 3 days for patients with:
        - Total daily doses >4 gm/day
        - On concurrent nephrotoxins (i.e. NSAIDs, loop diuretics, aminoglycosides, piperacillin/tazobactam, or amphotericin B).
        - Vancomycin trough levels maintained >15 mcg/mL
        - Concurrent vasopressor administration
      - NOTE: Urine output should be monitored as able along with evaluation of serum creatinine values.

- **Efficacy:**
  - The dosing pharmacist will assess the efficacy of therapy on a daily basis.
    - This evaluation will include the following as applicable: pertinent labs, intake/output, MD notes, nursing notes, culture results, vital signs, oxygenation (oxygen delivery method and oxygen supplementation needs), vasopressor requirements, and radiology reports.
Toxicity:
- The dosing pharmacist will assess for signs of nephrotoxicity on a daily basis.
  - See below “Nephrotoxicity” section for more information.

Situations in Which the Use of Vancomycin Should Be Discouraged:
- Routine surgical prophylaxis other than in a patient who has a life-threatening allergy to beta-lactam antibiotics
- Empiric antimicrobial therapy for a febrile neutropenic patient, unless initial evidence indicates that the patient has an infection caused by gram-positive microorganisms (e.g., at an inflamed exit site of Hickman catheter) and the prevalence of infections caused by MRSA in the hospital is substantial
- Treatment in response to a single blood culture positive for coagulase-negative staphylococcus, if other blood cultures taken during the same time frame are negative (i.e., if contamination of the blood culture is likely). Because contamination of blood cultures with skin flora (e.g., S. epidermidis) could result in inappropriate administration of vancomycin, phlebotomists and other personnel who obtain blood cultures should be trained to minimize microbial contamination of specimens
- Continued empiric use for presumed infections in patients whose cultures are negative for beta-lactam-resistant gram-positive microorganisms
- Systemic or local (e.g., antibiotic lock) prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters
- Selective decontamination of the digestive tract.
- Eradication of MRSA colonization
- Primary treatment of antibiotic-associated colitis
- Routine prophylaxis for very low-birthweight infants (i.e., infants who weigh less than 1,500 g (3 lbs 4 oz))
- Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis
- Treatment (chosen for dosing convenience) of infections caused by beta-lactam-sensitive gram-positive microorganisms in patients who have renal failure
- Use of vancomycin solution for topical application or irrigation.
PHARMACY VANCOMYCIN DOSING GUIDELINES
(Revised 6/2014)

GUIDELINES FOR DOSING AND MONITORING PATIENTS ON VANCOMYCIN

Background:
Vancomycin is a glycopeptides antibiotic that is active against aerobic and anaerobic gram-positive cocci. It is slowly bactericidal with a mechanism of action that consists of binding to peptidoglycan precursors and thus interfering with cell wall synthesis and repair. The pharmacodynamic parameter that best predicts the drug’s efficacy is free area under the time curve over the MIC (AUC:MIC ratio) of >400 mg*hr/L. Vancomycin has been in use since the 1950s; however, resurgence in use has been seen as a result of increasing rates of methicillin-resistant staphylococcus aureus (MRSA) in both the community and healthcare environments over the previous 20 years. Specific dosing of the drug has been the subject of debate over this time period with relatively regular alterations in dosing recommendations. The subject continues to evolve today.

Current ASHP/IDSA/SIDP guidelines for vancomycin dosing:

NOTE: This local guideline attempts to address several circumstances frequently encountered in the dosing and monitoring of vancomycin; however, given the vast inter-patient variability in vancomycin pharmacokinetics, it is not exhaustive by any means. Clinical judgment should be applied to each individual case and thought processes/dosing justification carefully documented.

- **Vancomycin Pharmacodynamics:**
  - Vancomycin efficacy (in the treatment of *Staphylococcus aureus*) is thought to most closely correlate with attainment of AUC:MIC ratios >400 mg*hr/L.
    - Given poor vancomycin penetration into certain tissues (i.e. bone, lungs, and blood-brain barrier penetration) and high protein binding (50-55%) an AUC:MIC >400 mg*hr/L may not be attainable if the organisms MIC is >1 mcg/mL depending on the site of infection.
  - E-tests should be ordered on MRSA isolated from the blood or CSF
  - Only vancomycin trough concentrations are recommended for ongoing monitoring of vancomycin therapy as, depending on the indication for therapy, trough goals of 10-15 mcg/mL or 15-20 mcg/mL have been shown to correlate with AUC:MIC ratios > 400 mg*hr/L.

- **Staphylococcus aureus and Vancomycin:**
  - Clinical Laboratory Standards Institute (CLSI) and the FDA have specified that *Staphylococcus aureus* with an MIC ≤ 2 mcg/mL are susceptible to vancomycin.
    - If MRSA with MIC ≥ 2 mcg/mL is encountered, regardless of method of susceptibility testing, the prescribing provider will be contacted and the pharmacist will recommend an alternative therapy as AUC:MIC >400 mg*hr/L is unlikely to be achieved without higher than standard doses and increased risk for nephrotoxicity.
    - **NOTE:** Current evidence (in adult patients and extrapolated to pediatrics) indicates that patients who are infected with organisms with MICs of 1.5-2 mcg/mL are slower to clear the organism, have longer durations of vancomycin therapy, are more likely to fail vancomycin therapy, and experience increased rate of mortality (mortality rate increase in studies driven by bloodstream infections as a source and organisms with Etest MIC of 2 mcg/mL).

- **Situations in Which the Use of Vancomycin Should Be Discouraged:**
  - Routine surgical prophylaxis other than in a patient who has a life-threatening allergy to beta-lactam antibiotics
  - Empiric antimicrobial therapy for a febrile neutropenic patient, unless initial evidence indicates that the patient has an infection caused by gram-positive microorganisms (e.g., at an inflamed
exit site of Hickman catheter) and the prevalence of infections caused by MRSA in the hospital is substantial.

- Treatment in response to a single blood culture positive for coagulase-negative staphylococcus, if other blood cultures taken during the same time frame are negative (i.e., if contamination of the blood culture is likely). Because contamination of blood cultures with skin flora (e.g., S. epidermidis) could result in inappropriate administration of vancomycin, phlebotomists and other personnel who obtain blood cultures should be trained to minimize microbial contamination of specimens.
- Continued empiric use for presumed infections in patients whose cultures are negative for beta-lactam-resistant gram-positive microorganisms.
- Systemic or local (e.g., antibiotic lock) prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters.
- Selective decontamination of the digestive tract.
- Eradication of MRSA colonization.
- Primary treatment of antibiotic-associated colitis.
- Routine prophylaxis for very low-birthweight infants (i.e., infants who weigh less than 1,500 g {3 lbs 4 oz}).
- Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis.
- Treatment (chosen for dosing convenience) of infections caused by beta-lactam-sensitive gram-positive microorganisms in patients who have renal failure.
- Use of vancomycin solution for topical application or irrigation.

- **Goal Vancomycin Troughs:**
  - Unless otherwise specified by the ordering provider, the dosing pharmacist will target the **below vancomycin goal troughs:**
    - All indications in adults will be maintained > 10 mcg/mL in order to prevent emergence of resistance and MIC creep.
      - **NOTE:** Exception may be AUC:MIC dosing strategies as outlined below under “Vancomycin Dosing in Special Patient Populations”.
    - **Trough goal = 15-20 mcg/mL:** *Staphylococcus aureus* bacteremia, endocarditis, meningitis, osteomyelitis/septic arthritis, necrotizing fasciitis, and hospital-acquired pneumonia caused by MRSA.
    - **Trough goal = 10-15 mcg/mL:** All other indications/organisms.
  - During therapy there may be an indication for a trough goal to be modified. The dosing pharmacist will contact the provider prior to adjusting goal vancomycin trough should this circumstance arise.

- **PAMC Recommended Calculator:**
  - Dose selection should be ordered based on appropriate weight based dosing and verified using population or patient specific parameters as appropriate.
    - The population/patient specific parameter based pharmacokinetic calculator to be used at PAMC is the Excel® calculator made available on the PAMC pharmacy intranet website.
      - Global RPh® is not to be used as a sole method for population based pharmacokinetic calculations as it does not appropriately round serum creatinine and may lead to inappropriately high initial dosing. Also, it requires the pharmacist to choose the desired vancomycin Vd. This may lead to inappropriate variation in dosing between pharmacists based upon value selected and the individuals knowledge of population estimates of vancomycin Vd.
      - **THE PAMC PHARMACOKINETIC CALCULATOR IS INTENDED TO AID WITH DECISION MAKING REGARDING VANCOMYCIN DOSING AND IS NOT INTENDED TO REPLACE CLINICAL JUDGMENT!!!**
      - **NOTE:** The calculator should NOT be used in patients with unstable renal function or patients with unpredictable/unstable volumes of distribution or clearance.
It should be noted that, based on currently published literature, the IDSA guideline dosing (utilization of actual body weight) may overestimate vancomycin needs in obese individuals.

- The PAMC vancomycin dosing calculator provides both mg/kg dose for both actual and adjusted body weight; however, dosing should be based on body weights specified below.
  - It has recently been shown that both initial empiric doses > 4 gm/day and body weight >100 Kg are risk factors for development of VIN. Both of these are likely to come into play in obese and morbidly obese individuals.

- **Population Parameter Calculations (as Programmed in the PAMC Vancomycin Calculator):**
  - Estimated CrCl:
    - \( CrCl \ (\text{ml/min}) = \frac{[(140-\text{Age})\times\text{IBW (kg)}]/[72\times\text{SCR}]\times(0.85 \text{ if female})}{\text{IBW}} \)
    - **NOTE:** Use AdjBW (as specified below) in place of IBW when patient is >120% of their IBW.
  - Ideal Body Weight (IBW):
    - Male: IBW (Kg) = 50 + 2.3*(Ht > 60 inches)
    - Female: IBW (Kg) = 45.5 + 2.3*(Ht > 60 inches)
  - Adjusted Body Weight (AdjBW):
    - AdjBW (Kg) = \[(\text{Total Body Weight} – \text{IBW})\times0.4\] + IBW

- **Procedure/Protocol Authority:**
  - Patient Selection/Consult Authority:
    - Pharmacy will initiate and modify vancomycin therapy for all patients admitted to the hospital upon receipt of the initial vancomycin order unless otherwise specified in the vancomycin order or if ordered by an Infectious Disease physician without a pharmacy to dose vancomycin consult.
    - The Infectious Diseases Clinical Pharmacy Specialist will evaluate all vancomycin regimens with doses >4 gm/day for appropriateness and opportunity for pharmacokinetic/pharmacodynamic dose optimization.
  - Laboratory Tests:
    - Per this guideline/protocol, the following laboratory tests may be ordered by a pharmacist in order to appropriately dose/monitor vancomycin usage.
      - Basic metabolic panel
        - BUN/SCR
          - **NOTE:** Baseline BUN/SCR MUST be obtained prior to scheduling of ongoing vancomycin regimen (i.e. must be obtained at minimum prior to 2nd dose).
      - Vancomycin levels (NOTE: Inpatient cost of vancomycin level is roughly $225)
        - Trough
        - Post-infusion
        - Random
        - **NOTE:** Even in non-consult patients on vancomycin, levels may be obtained as deemed clinically necessary by a monitoring pharmacist in order to appropriately monitor for toxicity development.
  - Vancomycin Etest on MRSA isolates obtained from blood or CSF.

- **Vancomycin Administration Times:**
  - **Usual Administration Times:**
    - \( \leq 1000 \text{ mg}: \text{Infuse over 1 hour} \)
    - \( 1250-1500 \text{ mg}: \text{Infuse over 1.5 hours} \)
    - \( 1750-2000 \text{ mg}: \text{Infuse over 2 hours} \)
    - \( >2000 \text{ mg}: \text{Infuse over 3 hours} \)
    - **NOTE:** Infusion times longer than those listed above may be used per the pharmacist’s judgment in pediatric patients depending on dose and/or if “redman syndrome” occurs with the above infusion times.
• **Initial Assessment:**
  o Initial assessment of vancomycin dosing by the dosing pharmacist should include review of all of the following:
    ▪ Indication for usage and severity of infection
      • Vital signs (i.e. respiratory rate, heart rate, blood pressure)
      • Signs of end organ damage (i.e. altered mental status, increased SCr, lactate >4, increased LFTs, etc.)
      • Physical findings (i.e. description of cellulitis, description of pulmonary status, etc)
    ▪ Known medication allergies
    ▪ Height/Weight
    ▪ Available/pertinent labs
      • BUN/SCr
        o NOTE: SCr must be assessed prior to scheduling an ongoing vancomycin regimen
      • WBC
      • Inflammatory markers (ESR, CRP, and procalcitonin)
      • Vancomycin troughs (if coming from outside facility)
    ▪ Available cultures
      • Both current and from recent hospitalizations if applicable
        o NOTE: Whenever possible, encourage cultures to be taken prior to antibiotic administration, but do not delay therapy in septic patients as every hour antimicrobials are delayed in patients with septic shock may increase the odds of mortality by up to 7.6%
    ▪ Available radiology/procedure reports
    ▪ Pertinent past medical history
      • Co-morbid conditions (i.e. CHF, CKD, ESRD, etc)
      • Recent hospitalizations
      • Social history (i.e. IVDU, residence in ALF, etc)
      • Anticipated duration of therapy

• **Initial Adult Vancomycin Dosing:**
  o Initial Vancomycin Dose Selection (Use “Vanco Initial Dosing” Tab in Calculator):
    ▪ **Loading DOSE Recommendations:**
      • In critically ill patients, loading doses may be used to achieve target trough concentrations more quickly than standard dosing regimens.
        o Critical illness: bacteremia, endocarditis, meningitis, osteomyelitis/septic arthritis, suspected necrotizing fasciitis, hospital acquired pneumonia caused by methicillin resistant *Staph. Aureus*, severe sepsis, or as specified by prescriber.
          ▪ **NOTE:** Severe sepsis is defined as meeting SIRS criteria + evidence of infection + end organ damage.
        ▪ **SIRS Criteria:**
          o Temperature: >38C or <36C
          o HR >90 bpm
          o RR >20 or pCO2 < 32
          o WBC >12K or <4K
        ▪ **End organ damage:**
          o LFT elevation
          o SCr elevation
          o Altered mental status
          o Elevated serum lactate
          o **NOTE:** Loading doses are NOT necessary for all indications and should be reserved to the above indications.
      • Recommended Dose:
o Patient’s ABW <120% of IBW:
  ▪ 25-30 mg/kg x 1 dose based on actual body weight.
  ▪ Max 3 grams.
o Patient’s ABW >120% of IBW:
  ▪ 25-30 mg/kg x 1 dose based on adjusted body weight.
  ▪ Max 3 grams.
o Patients > 150 Kg:
  ▪ See serial kinetic section below

**Maintenance DOSE Recommendations:**
- Patient’s ABW <120% of IBW:
  o 15-20 mg/kg/dose based on actual body weight.
  ▪ Max 2 grams
- Patient’s ABW ≥120% of IBW:
  o 15-20 mg/kg/dose based on adjusted body weight as calculated above.
  ▪ Max 2 grams
- Patients > 150 Kg:
  o See serial kinetic section below.

**Initial Maintenance INTERVAL Selection:**
- Normal renal function (CrCl > 90 ml/min): q8-12hrs
- Mild renal impairment (CrCl 50-90 ml/min) or age >60 y/o: q12-24hrs
- Moderate renal impairment (CrCl 20-49 ml/min): q24hrs
- Severe renal impairment (non-HD): Interval determined by serum vancomycin levels
  o May be unable to schedule a “regular” maintenance interval (i.e. “dose by levels” for duration of therapy).

**Adjustment of Vancomycin Dosing Based on Trough Levels:**
- **Adjustment of Vanco Dosing:**
  ▪ *NOTE:* Vancomycin dosing may be adjusted based on a single level; however, this requires the utilization of at least one population based pharmacokinetic parameter in the estimation of a more patient specific elimination rate constant. In the case of the PAMC calculator the retained population pharmacokinetic parameter is the volume of distribution.
  ▪ Trough levels should be obtained at steady state (just prior to the 4th or 5th vancomycin dose) in most circumstances; however, circumstances do exist when earlier levels may be necessary (i.e. concern for toxicity or unstable renal function).
  ▪ *NOTE:* When levels are obtained and the regimen is NOT at steady state this should be taken into consideration and noted in communication to providers and other pharmacists (i.e. progress notes, interventions, and handoff).

**Procedure:**
- Stable Renal Function (Use "Vanco Dose Adjustment" Tab in Vanco Calculator):
  o Obtain a trough level at steady state and roughly 0.5 hour prior to the dose.
  o PAMC Vancomycin Calculator:
    ▪ Step 1: Input data for population kinetic parameter calculation (namely Vd in this circumstances).
    ▪ Step 2:
      ▪ Input dosing regimen, trough level, and level timing.
      ▪ Note true trough obtained.
      ▪ Note estimated AUC(0-24).
    ▪ Step 3:
      ▪ Input desired peak/trough
      ▪ Note recommended dosing regimen based on previously input desired peak/trough
• Select dose that provides most appropriate trough and estimated AUC(0-24).
  ▪ Step 4:
    • Input previous/future dosing into chart if desired for visual aid/graph for progress note.
      o NOTE: This graph/strategy may be useful with regards to determining when to initiate the new regimen based on the trough level obtained if regimen adjustment involves lengthening the dosing interval.
  ▪ Stable, impaired renal function:
    • If two levels on the same vancomycin elimination curve are obtained AND serum creatinine is elevated but stable, the “Vanc Renal Non-HD” tab of the vancomycin calculator may be used to determine a patient specific elimination rate constant and potentially a regularly scheduled dosing interval or estimated time to next dose.
  ▪ Unstable Renal Function:
    o Obtain troughs as clinically indicated based on fluctuations in renal function in order to minimize toxicity/assure appropriate trough/AUC(0-24) being attained.
    o Clinical judgment is necessary with regards to when to obtain troughs, evaluation of levels, and dosing adjustment in patients with unstable renal function.
      • NOTE: Vancomycin calculator may be used for ROUGH ESTIMATION of parameters/levels in these patients; however, should be used EXTREMELY CAUTIOUSLY as it assumes stable renal function!

• Vancomycin Dosing in Special (ADULT) Patient Populations:
  o Vancomycin Dosing in Pregnant Patients or Patients Within 30 Days of Delivery:
    ▪ Pregnant patients have an elevated volume of distribution as compared to other adult populations. This volume of distribution will typically return to normal within roughly 14 days of delivery; however, may remain elevated for as long as 30 days after delivery.
    ▪ Pregnant patients and those who have delivered within the previous 30 days should be dosed within the above listed dosing ranges for adults; however, the upper end of the dosing range, or more frequent dosing may be considered given the alternation in pharmacokinetic parameters in these patients (i.e. elevated Vd).
  o Serial Vancomycin Kinetics (Use “Vanco Serial Initial” Tab on PAMC Vanco Calculator):
    ▪ Due to variations in vancomycin pharmacokinetics in the morbidly obese patient population PAMC guidelines recommend serial vancomycin pharmacokinetics be performed in order to rapidly obtain patient specific dosing parameters.
      • By obtaining two levels on the same elimination curve a patient specific elimination rate constant, half-life, volume of distribution, and clearance can be calculated thus allowing for more accurate dosing.
      • Serial kinetics should only be performed on patients with stable renal function.
      • NOTE: When serial vancomycin kinetics are performed an AUC:MIC ratio may be useful in guiding dose selection given the utilization of patient specific pharmacokinetic parameters; however, the trough (with goals as above) remains the primary vancomycin target unless otherwise recommended to provider who is in agreement with AUC:MIC kinetics per below AUC:MIC dosing strategy.
    ▪ Procedure:
      • Order an appropriate dose:
If loading dose desired: 3 grams
If no loading dose desired: 15 mg/kg x 1 dose using adjusted body weight. Max 3 grams.

- Infusion Time: 3 hours (or as appropriate if no loading dose necessary)
- Serial levels:
  - 1st level: 3 hours after the end of a 3 hour infusion
  - 2nd level: 6 hours after the 1st level was obtained
- Input levels into the calculator in order to generate patient specific parameters.
- Use these calculated parameters to calculate dose anticipated to produce peak ~30 mcg/mL and trough within desired range.

Vancomycin Dosing in Hemodialysis:

- **Initial Dosing:**
  - Patients <120% of IBW:
    - 15 mg/kg x 1 dose based on actual body weight
      - Max 2 grams
  - Patients ≥120% of IBW:
    - 15-20 mg/kg x 1 dose based on adjusted body weight as calculated above
      - Max 2 grams

- **Maintenance Dosing:**
  - Vancomycin is 39% +/- 13% removed by high flux hemodialysis membranes.
    - *NOTE: Some hemodialysis patients retain minimal urine output. This slow, additional elimination of the drug must be considered when applicable during hemodialysis dosing.*
  - Vancomycin levels should be obtained prior to the dialysis session after the 1st post dialysis dose.
    - i.e. Loading dose $\rightarrow$ dialysis $\rightarrow$ post-dialysis dose $\rightarrow$ level $\rightarrow$ dialysis $\rightarrow$ new post-dialysis dose
    - Vancomycin levels should be drawn just PRIOR TO hemodialysis in order to assess the level at which the patient has been maintained throughout the intradialytic period.
  - Patient should be re-dosed when the serum vancomycin concentration post-hemodialysis is anticipated to be below the lower limit of the goal trough range.
    - Typical post-dialysis doses will be 500-1000 mg after each dialysis session.
      - Doses >1000 mg after each dialysis session are not likely to be necessary unless the patient has retained significant urinary output.

Hemodialysis and Vancomycin Epic Order Specifics:

- When ordering a vancomycin trough call the dialysis unit to determine when the patient is to dialyze.
  - Order the trough at 0800 for AM session and 1200 for PM sessions with the order comment, “TO BE DRAWN JUST PRIOR TO DIALSYS”.
  - Notify the hemodialysis RN that pharmacy will be ordering a trough and be sure they know they will need to draw it. They will make note of this on the whiteboard in the unit to communicate this information to the other HD nurses.

- When placing vancomycin drug orders for hemodialysis patients the drug must be ordered with the order frequency “After Each Dialysis” and a “dialysis” phase of care must be entered at order verification in order to assure that the dialysis RN will see the order in the “Dialysis” tab of the medication administration record and subsequently administer the medication.
  - *This order will be discontinued by the hemodialysis RN at the end of every dialysis session and will need to be reordered by the*
pharmacist each time. Careful attention should be paid to these orders to prevent the patient from missing doses.

- Vancomycin Dosing in Continuous Renal Replacement Therapy:
  - Clearance:
    - Clearance of vancomycin is highly dependent on the method of CRRT, the filter type, and the flow rate. Patients should be monitored closely for clinical improvement, adverse reactions, and drug accumulation (i.e. levels).
    - **NOTE:** These recommendations are based on dialysate flow rate of 3 L/hr, an total effluent rate of 0-1 L/hr, and no residual renal function.
      - PAMC utilizes CVVH (most common), CVVHD, or CVVHDF via the NxStage® dialyzer.
  - Initial Dosing:
    - Loading Dose:
      - Patients <120% of IBW:
        - 20-25 mg/kg x 1 dose based on actual body weight
        - Max 3 grams
      - Patients ≥120% of IBW:
        - 20-25 mg/kg x 1 dose based on adjusted body weight as calculated above
        - Max 3 grams
    - Maintenance Dose:
      - Patients <120% of IBW:
        - 15 mg/kg (actual body weight) IV q24hrs
        - Max 2 grams
      - Patients ≥120% of IBW:
        - 15 mg/kg (adjusted body weight) IV q24hrs
        - Max 2 grams
  - Ongoing Maintenance Dosing:
    - Vancomycin levels should be obtained prior to the 4th total vancomycin dose assuming CRRT continues to that point.
      - Changes in method of renal replacement therapy will drastically alter vancomycin clearance. Changes in type of renal replacement (i.e. CRRT to HD or CRRT to no renal replacement) should prompt re-evaluation of dosing and utilization of early level after the change to avoid toxicity due to accumulation.
      - Given the continuous nature of CRRT vancomycin levels should be obtained 30 minutes prior to the next schedule dose.
      - Vancomycin target trough goal do not change and are as listed above.

- AUC:MIC Kinetics (Use “AUC to MIC Ratio Dosing” Tab on PAMC Vanco Calculator):
  - General Information:
    - Vancomycin goal troughs as specified by IDSA has been determined as they appear to most closely correlate with an AUC:MIC ratio of >400 mg*hr/L in the general population. Use of these troughs may overestimate AUC:MIC ratio produced in certain patients, therefore making calculation of a patient specific AUC:MIC ratio important to avoid unnecessary overexposure to vancomycin and minimize the incidence of nephrotoxicity.
      - AUC:MIC pharmacokinetics are NEVER to be performed without the prescribing physician’s understanding and approval of the dosing strategy.
    - AUC:MIC dosing should only be considered for recommendation to the physician if the patient meets all of the following criteria:
      - Stable renal function
      - Anticipated duration of therapy >14 days
- Total vancomycin need (as verified by initial levels) ≥4 gm/day
- AUC:MIC dosing is NOT appropriate in individuals with the following:
  - CNS infection
  - Unstable renal function
  - Hemodialysis or CRRT patients
- In order for most accurate calculation of AUC:MIC ratio the vancomycin regimen should be at steady state when levels are obtained.
- Utilization of MIC:
  - AUC:MIC ratio goal of >400 mg*hr/L was established in *Staphylococcus aureus* bloodstream infections and pneumonia, but has not been studied in other indications or organisms.
  - Given MIC distribution listed above under “*Staphylococcus aureus* and vancomycin” paired with logistics of dosing and safety, an MIC of 1 mcg/mL should be utilized for dosing to an AUC:MIC ratio when an MIC is not available or when the MIC of the *S. aureus* isolated is 0.5 mcg/mL.
  - If both VITEK and Etest MICs are available the Etest MIC should be utilized for AUC:MIC dosing.
    - NOTE: For organisms with an MIC >1 mcg/mL adverse outcomes with regards to failure of therapy and increased mortality have been observed as mentioned above under “Pharmacodynamics”. When the MIC is >1 an AUC:MIC >400 mg*hr/L is often difficult to obtain and either:
      - Alternative therapy should be considered
        - Daptomycin
        - Linezolid
        - Ceftaroline
        - Clindamycin
        - Sulfamethoxazole/Trimethoprim
        - Doxycycline
        - Tedizolid
        - Dalbavancin
  - Vancomycin should be utilized and optimized as appropriate while taking into consideration both the risk of continued use of vancomycin with regards to literature documented patient outcomes and safety/toxicity of the regimen necessary to obtain AUC:MIC ratios of 400 mg*hr/L.
- **Procedure:**
  - **Levels:**
    - While at steady state obtain two levels as below:
      - **Post-infusion level:** 1 hour after the end of the infusion
      - **Trough level:** 0.5 hour prior to the next infusion
    - NOTE: Two levels are needed for AUC:MIC calculation and ideally they would occur on the same elimination curve; however, as long as regimen is at steady state a trough level may be obtained before a dose, the dose then given, and a post-infusion level obtained 1 hour after the infusion is completed if this is easier logistically with regards to level timing, pharmacist staffing, etc.
    - NOTE: Level timing as above is ideal; however, as long as timing of levels is taken into consideration with regards to calculating Kel and extrapolating peaks and troughs, timing of levels is NOT imperative (i.e. two levels obtained on a steady state elimination curve after distribution phase of the dose is complete is all that is needed).
  - Input vancomycin dosing regimen (dose, interval, and infusion time), levels, and appropriate level timing into the PAMC vancomycin calculator as appropriate.
Step 1: Calculator will use levels to calculate a Kel, back extrapolate a true peak, forward extrapolate a true trough, and then calculate an AUC(0-24hrs).

Step 2: Choose a new dosing regimen.
- Calculator will use previously calculated (patient specific) Kel to estimate peak/trough and AUC(0-24).
- NOTE: Given literature with regards to MRSA bloodstream infections showing AUC:MIC ≥ 421 mg*hr/L being associated with less treatment failure and natural variation in Kel (not a completely constant process) it is wise to target an AUC(0-24) of ~475 mg*hr/L.
  - This is based on AMS Pharmacist experience with dosing strategy and not on published evidence (not available).
- Once regimen is altered allow new regimen to achieve steady state then obtain repeat levels in order to verify AUC(0-24) target is being achieved.
- Make note of trough which must be achieved in order to assure an AUC:MIC >400 mg*hr/L be attained.
  - NOTE: In most circumstances use of AUC:MIC kinetics will simply allow for target trough goal to be reduced to 10-15 mcg/mL for indications in which guidelines would specify higher trough goal be targeted.
- Once AUC(0-24) of regimen has been confirmed then troughs should be monitored weekly for development of toxicity and to assure that troughs remain greater than previously specified minimum trough goal necessary to attain AUC(0-24) target.
- Clear communication to providers (via progress notes), pharmacists (via handoff, progress notes, and iVents), and outside facilities at transition of care is necessary to assure the process functions smoothly.
  - Questions regarding AUC:MIC pharmacokinetic dose optimization should be directed at the ID Clinical Pharmacy Specialist.

**NEONATAL Vancomycin Dosing:**
- **Goal Vancomycin Troughs:**
  - Trough goal = 15-20 mcg/mL: *Staphylococcus aureus* bacteremia, endocarditis, meningitis, osteomyelitis/septic arthritis, necrotizing fasciitis, and hospital-acquired pneumonia caused by MRSA.
  - Trough goal = 10-15 mcg/mL: All other indications/organisms.
  - NOTE: Lower goal trough as mentioned below in PEDIATRIC section does not apply to neonates and optimal AUC:MIC targets have not been studied in neonates. AUC:MIC dosing is not to be performed in this patient population.

- **Initial Dosing:**
  - 10-15 mg/kg/dose (all ages with normal renal function) for all indications
  - Interval is determined by age related renal function (see table below):

<table>
<thead>
<tr>
<th>Postmenstrual Age (wks)</th>
<th>Postnatal Age (days)</th>
<th>Interval (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>0-14</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>&gt;14</td>
<td>12</td>
</tr>
<tr>
<td>30-36</td>
<td>0-14</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>&gt;14</td>
<td>8</td>
</tr>
<tr>
<td>37-44</td>
<td>0-7</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>&gt;7</td>
<td>8</td>
</tr>
<tr>
<td>&gt;45</td>
<td>All</td>
<td>6</td>
</tr>
</tbody>
</table>

- **Obtaining Troughs:**
- Obtain levels as per “Obtaining Vancomycin Troughs” section below.

**PEDIATRIC Vancomycin Dosing:**

- **Pharmacokinetic Parameters Unique to Pediatrics:**
  - **Vancomycin Renal Elimination**
    - Pediatric patients 6 months to 12 years eliminate vancomycin at roughly twice the rate as adult patients.
    - Newborns typically eliminate vancomycin similarly to or slower than do adult patients.
      - Estimated vancomycin terminal half-lives:
        - Newborns: 6-10 hours
        - 3 months – 3 years: 4 hours
        - >3 years: 2.2-3 hours
        - Adults: 5-8 hours
  - **Goal Vancomycin Troughs (age 3 months – 18 years):**
    - **Trough goal = 10-15 for all indications/organisms**
      - Higher trough goals (15-20 mcg/mL) may be considered for patients with *Staphylococcal* meningitis or VP shunt infection; however, vancomycin serum levels may not correlate well with CSF levels given poor penetration. Little evidence exists regarding use of serum vancomycin levels as predictors of success in this infection type. Infectious Diseases and Neurosurgery should be consulted and intraventricular vancomycin should be considered.
    - **NOTES:**
      - During therapy there may be an indication for a trough goal to be modified. The dosing pharmacist will contact the provider prior to adjusting goal vancomycin trough should this circumstance arise.
      - Given the more frequent administration of vancomycin in pediatric patients (typically q6hr or q8hr interval) AUC(0-24) of 400 mg*hr/L may be attained by targeting lower trough goals than those previously specified in the available IDSA guidelines.
        - Available evidence suggests that vancomycin troughs of 7-10 mcg/mL should be sufficient to produce AUC(0-24) of 400 mg*hr/L in 90% of patients.
      - **AUC:MIC Dosing in pediatric patient is likely a more appropriate dosing strategy and should be considered on a case by case basis (i.e. anticipated long duration of therapy, large doses required (as verified by levels), and in patients with stable renal function).**
        - See above section for AUC:MIC dosing

- **Initial Dosing:**
  - Age: 1 month (and post-menstrual age >44 weeks) – 12 years:
    - 15 -20 mg/kg/dose IV q6hrs (60-80 mg/kg/day)
  - Age: 12 years – 18 years:
    - 15-20 mg/kg/dose IV q6-8hrs (45-80 mg/kg/day)
    - Interval in renally impaired pediatric patients determined on case by case basis based on SCr and UOP.

- **Obtaining Troughs:**
  - Vancomycin trough levels should be obtained according to the same standards outlined below.

**Obtaining Vancomycin Troughs (Adults, NEONATES, AND Pediatrics):**

- **Timing in Relation to Dose:**
  - Draw trough within 30 minutes prior to the next dose.

- **Initial Troughs:**
  - Obtain trough when vancomycin steady state is achieved (i.e. just prior to 4th dose of vancomycin (including loading dose)).
- **NOTE:** True steady state is achieved at 4-5 drug elimination half-lives (i.e. roughly 4-5 vancomycin doses); thus, if level is obtained just prior to 4th dose, a relatively small degree of accumulation may occur with ongoing administration of the currently ordered regimen.

- In some patients vancomycin troughs may not be needed. If patient’s meet ALL of the below criteria they may be eligible to NOT have trough levels drawn.
  - Anticipate duration of therapy <5 days
  - No vancomycin induced nephrotoxicity risk factors
    - See “Nephrotoxicity” section below
  - Indication warranting goal trough target of 10-15 mcg/mL

  - **Ongoing:**
    - Obtain trough levels just prior to 4th dose (i.e. when concentration steady state has been reached) of new regimens as appropriate when previous regimen is changed in response to subtherapeutic or supratherapeutic vancomycin level.
    - Troughs should be drawn weekly at minimum throughout prolonged therapy in hemodynamically stable patients.
      - Troughs need to be drawn more often (every 3-5 days at minimum) in:
        - Hemodynamically unstable patients
        - Those with rapidly changing/unstable renal function
          - Patient with worsening renal function may need to be evaluated for likelihood of development of vancomycin induced nephrotoxicity.
        - Ongoing use/addition of concurrent nephrotoxin (i.e. NSAIDs, loop diuretic, aminoglycoside, piperacillin/tazobactam, or amphotericin B).

- **Obtaining Labs for Monitoring:**
  - **Serum Creatinine (SCr) should be obtained:**
    - **At baseline:**
      - **NOTE:** Baseline BUN/SCr MUST be obtained prior to scheduling of ongoing vancomycin regimen (i.e. must be obtained at minimum prior to 2nd dose).
    - **Ongoing:**
      - Weekly at minimum in patients on vancomycin
      - Daily in patients with unstable renal function
      - At least every 3 days for patients with:
        - Total daily doses >4 gm/day
        - On concurrent nephrotoxins (i.e. NSAIDs, loop diuretics, aminoglycosides, piperacillin/tazobactam, or amphotericin B).
        - Vancomycin trough levels maintained >15 mcg/mL
        - Concurrent vasopressor administration
      - **NOTE:** Urine output should be monitored as able along with evaluation of serum creatinine values.

- **Efficacy:**
  - The dosing pharmacist will assess the efficacy of therapy on a daily basis.
    - This evaluation will include the following as applicable:
      - Pertinent labs
      - MD notes
      - Nursing notes
      - Culture results
      - Vital signs
      - Oxygenation, oxygen delivery method, and oxygen supplementation needs
      - Vasopressor requirements
      - Radiology reports
      - Intake and output
Should culture data become available that allows for the streamlining/de-escalation of antimicrobials the dosing pharmacist or AMS pharmacist will contact the appropriate provider and give recommendations for ongoing therapy.

- **NOTE:** Available literature (primarily in bloodstream infections) indicates beta-lactam therapy is more effective (less treatment failure, shorter duration of hospital stay, and lower mortality rate) than vancomycin therapy for the treatment of MSSA.

In slow to respond/non-responding patients being treated for severe MRSA infections and/or MRSA infections in difficult to penetrate tissue (meningitis, endocarditis, bacteremia, osteomyelitis, septic joints, and pneumonia) and the organism has a VITEK reported MIC of ≥1 mcg/mL an Etest may be of benefit.

- If the Etest MIC returns >1 mcg/mL transition to alternate therapy or more aggressive vancomycin dosing may be needed to assure AUC:MIC >400 mg*hr/L are being reached.
  - May consider AUC:MIC dose optimization if vancomycin to be used.
  - **NOTE:** The Etest MIC is potentially more accurate with regards to true MIC and correlates to outcomes/measurements from available literature (primarily MRSA bloodstream infection studies) regarding vancomycin efficacy. The VITEK 2 automated microbroth dilution instrument may underestimate the MIC of MRSA isolates by:
    - One microbroth dilution in ~ 50% of isolates with a true MIC of 1 mcg/mL
    - 1-2 microbroth dilutions in ~20% of isolates with a true MIC of 2 mcg/mL

**Documentation:**

- **Progress Notes:**
  - **Initial Progress Note:**
    - An initial pharmacy to dose vancomycin consult note will be written by either the pharmacist doing the initial dosing or if ordered overnight the pharmacist assuming care in the morning after the consult was placed.
    - This progress note will contain, at minimum:
      - Indication for vancomycin
      - A brief description of clinical course to this point
      - MRSA history (if applicable)
      - Target trough
      - Additional antimicrobials
      - Current plan/dosing regimen
      - Patient height/weight (and adjusted body weight if applicable)
        - The weight used for dosing will be indicated
      - Pertinent laboratory values
        - WBC
        - % bands
        - BUN/SCr
        - Inflammatory markers (ESR, CRP, and procalcitonin)
        - Any previous applicable vancomycin troughs
      - Intake/Output
      - Vital signs
      - Vasopressor administration (if applicable)
      - Estimated CrCl
      - Available microbiology
        - Including vancomycin MIC if MRSA isolated
      - A brief description of available and pertinent radiology reports and/or procedures performed

- **Monitoring Progress Note:**
  - Ongoing monitoring progress notes will be written by the dosing pharmacist as indicated by change in patient status, change in renal function, levels obtained, dose adjustment, or microbiology updates.
  - This note will contain, at minimum:
Any vancomycin levels obtained
Any current dosing changes
Plan for next trough level
Pharmacist’s perceived assessment of efficacy (if concerned)
Pharmacist’s perceived assessment of toxicity (if concerned)
Pertinent labs (as defined above)
Updated available microbiology

**NOTE:** Neither initial nor monitoring vancomycin progress notes need be written for vancomycin consultation involving surgical prophylaxis for which the anticipated duration of therapy is ≤48hrs.

**Adverse Event Reporting:**
- All adverse events pertaining to the administration of vancomycin should be entered as an ADR iVent +/- UOR is appropriate.
- Reasonable indications for documentation of adverse events includes:
  - Redman’s syndrome
  - Vancomycin induced nephrotoxicity (VIN)
    - Please document all cases where patient is on vancomycin and SCr increases >0.5 mg/dL from baseline or 50% from baseline for two consecutive days as possible VIN and report them to the ID Pharmacist
  - Unexplained neutropenia
  - Unexplained thrombocytopenia
  - Extravasation of the drug
  - For all true trough levels >25 mcg/mL resulting from regularly scheduled vancomycin the AMS pharmacist should be notified.

**Nephrotoxicity:**
One of the primary toxicity concerns with regards to vancomycin has been possible associated nephrotoxicity. Initially, the high rates of nephrotoxicity were attributed to impurities in earlier formulations and after resolution of this issue nephrotoxicity was reported to occur at rates of <5%. New, more aggressive guidelines, with regards to dosing and target troughs, were released in 2009 by the Infectious Disease Society of America (IDSA) and available literature since this time has reported vancomycin induced nephrotoxicity (VIN) rates as high as 43% and as low as 5%. VIN is typically reversible. One study in adult medicine patients noted that VIN most typically occurred around 2-5 days into therapy, peaked at 5-10 days, and resolved within 19 days. A meta-analysis, published in 2013, found VIN to occur 4.3-17 days after the initiation of therapy. They also found that most patients renal function resolved within 7 days of discontinuation of vancomycin and only 3% of VIN patients were found to require short-term hemodialysis. They also found VIN to be associated with increasing length of hospitalization, length of ICU stay, and overall mortality.

In the adult population risk factors for VIN include:
- Concurrent exposure to other known nephrotoxins
  - Amphotericin
  - Aminoglycosides
  - IV contrast
  - Loop diuretics
  - Piperacillin/tazobactam
- Adult Critical Care Admission
- Vasopressor administration
- Weight ≥ 101 Kg
- History of acute or chronic kidney injury
- Empiric vancomycin doses >4 gm/day
- Prolonged courses (>5 days)
- Unstable renal function
- Initial (within 96 hrs) vancomycin trough concentration (controversial data)
  - Highest incidence: >20 mcg/mL
  - Lowest incidence: <10 mcg/mL
In the pediatric population VIN has been shown to occur at a rate of 5.4-14%; however, this data is limited to a few small studies. There is conflicting evidence regarding whether or not the trough levels have an impact on the occurrence of VIN.

Risk factors reported in studies which have shown to increase the risk of VIN in the pediatric population include:

- Longer durations of therapy (≥7 days)
- Use of extracorporeal membrane oxygenation (ECMO)
- Use of vasopressors
- PICU admission
- Concurrent loop diuretic exposure
- Trough levels >15 mcg/mL (conflicting evidence)

Patients with the above risk factors (both adult and pediatric) should be closely monitored for VIN as per the below definition.

- **VIN definition:**
  - An increase of >0.5 mg/dL (or a 50% increase from baseline whichever is greater) in consecutively obtained daily SCr values
  - A drop in calculated CrCl of 50% from baseline on two consecutive days without another reasonable explanation

The dosing pharmacist should assess the renal function of every patient receiving vancomycin daily. This evaluation should include monitoring for GFR/CrCl, SCr, BUN, and urine output (volume and/or documented unmeasured voids). Additionally, each patient’s MAR should be monitored daily for the initiation of nephrotoxins (as listed above).

When the pharmacist responsible for the vancomycin dosing suspects VIN (as per the above definition) the provider should be contacted for further instruction and the AMS pharmacist notified.

**Ototoxicity:**

Vancomycin induced ototoxicity is controversial. No evidence of vancomycin induced hearing loss has been observed in animal models and again early studies suggested that vancomycin induced ototoxicity may have actually been caused by impurities in the formulation. These studies also suggest that there may be additive ototoxicity when vancomycin is used in conjunction with aminoglycosides. These older studies estimate that ototoxicity with vancomycin occurs at a rate of 1-9% and correlated most closely with serum vancomycin concentrations >40 mcg/mL.

Today, the actual occurrence of vancomycin induced hearing loss with vancomycin monotherapy is rare; however, data is limited after release of guidelines targeting more aggressive troughs. Ototoxicity has not been shown to correlate well with serum vancomycin concentrations. The hearing loss is characterized by the damage of the auditory nerve and is usually irreversible. It most commonly presents with the loss of high-frequency tones and/or tinnitus and then slowly progresses to loss of mid-tone, low-tones, and eventual total deafness.

Vancomycin levels need not be monitored to prevent ototoxicity; however, patients receiving concurrent aminoglycosides should be monitored most closely for hearing loss. If the pharmacist managing the vancomycin determines that the patient is experiencing tinnitus or high frequency hearing loss the provider should be contacted for further instruction and the AMS pharmacist notified.

**REFERENCES:**

7. Lodise TP, Lomaestro B, Graves J, Drusano GL. Larger vancomycin doses (at least four grams per day) are associated with an increased incidence of nephrotoxicity. Antimicrob Agent and Chemother 2008;52(4):1330-1336.