MEDICATION MONITORING:
Pharmacist-Managed Intravenous (IV) Vancomycin Protocol

I. PURPOSE

To allow standardized pharmacist management of IV vancomycin in the inpatient setting using evidence-based guidelines and best practices.

II. POLICY

Upon physician request, SHC pharmacists will manage IV vancomycin therapy in accordance with evidence-based guidelines and best practice standards.

- Adjust vancomycin orders
- Order pertinent labs (e.g. vancomycin levels, SCr)
- Provide documentation via progress notes and Epic flowsheet

Protocol exclusions:
1. One-time dose
2. Surgical/peri-operative prophylaxis
3. Pediatric patients (<18 years of age)

III. PROCEDURES

A. Physician Responsibility

1. Indicate that a patient is to receive vancomycin according to this protocol by entering an order for “Vancomycin per Protocol” and specifying the following:
   a. Initial indication: Prophylaxis, empiric, definitive
   b. Suspected infection type
   c. Anticipated duration of therapy
   d. Goal trough level (recommendations below)

   Table 1. Goal Trough Levels by Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Goal Trough (mcg/ml)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis, skin/soft tissue infections not penetrating bone</td>
<td>10 – 15</td>
</tr>
<tr>
<td>Pneumonia, Staphylococcus Aureus bacteremia, endocarditis, osteomyelitis,</td>
<td>15 – 20</td>
</tr>
<tr>
<td>deep seated infections, meningitis, sepsis, necrotizing fascitis, febrile</td>
<td></td>
</tr>
<tr>
<td>neutropenia (for suspected/proven MRSA or severe infection)</td>
<td></td>
</tr>
</tbody>
</table>

   Trough levels >10 mcg/ml are recommended to avoid microbial resistance.
   ** Goal trough of 15-20 assumes targeting MRSA. Limited data on target troughs for non-Staphylococcus Aureus infections

2. Continue to follow vancomycin levels. Consult with the pharmacist as needed.
3. Notify the pharmacist of acute changes in patient’s status that may impact vancomycin dosing (e.g. changes in renal function or urine output).
4. The physician may discontinue and/or reinitiate the protocol at any time.
   a. If the protocol is discontinued, the physician assumes responsibility for vancomycin therapy management

B. Pharmacist Responsibility (contents of this section appears in other parts of the document—consider limiting it to strictly procedural responsibilities vs. clinical assessment?)

1. Upon receipt of a “Vancomycin per Protocol” order, review the patient’s chart to ensure the appropriate use of vancomycin.
   a. Review allergies
   b. If the indication is not provided and/or not clear in the chart, contact the physician for clarification
c. If vancomycin use is not appropriate, contact the physician to provide recommendations for alternative therapies

2. Prior to initiating therapy, obtain a current patient height, weight, and serum creatinine.

3. After reviewing the patient’s chart, write the necessary lab and medication orders for vancomycin therapy.
   a. Sign all orders as “Per Protocol without co-sign” with the ordering pharmacist’s name.

4. Documentation
   a. Document daily review of patient’s chart and vancomycin dosing in the pharmacy flowsheet.
   b. Enter a daily Pharmacy Progress Note using the Pharmacy Monitoring note template (“vancomycin”)

IV. DOSING & MONITORING GUIDELINES
(Disclaimer: The following guidelines do not preclude clinical judgment.)

A. Initial Dosing
1. Review the following prior to initiation of therapy:
   a. Indication
   b. Age, gender, height, weight, BMI
   c. Relevant and pending microbial culture(s)
   d. Renal replacement therapy
   e. Special populations (obese, elderly, severely malnourished [BMI<16], amputees, pregnancy)
   f. Serum creatinine (SCr), urine output (if available), creatinine clearance (CrCl)
      i. Calculate CrCl using the Cockroft-Gault equation (Figure 1)
         a) Elderly or severely malnourished: consider rounding SCr—clinical discretion advised

<table>
<thead>
<tr>
<th>Wt &lt; 40kg or age &gt; 65 and:</th>
<th>Round SCr to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCr ≤ 0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>SCr 0.5 - 1</td>
<td>1</td>
</tr>
</tbody>
</table>

b) Use ideal body weight (IBW) for non-obese patients

c) Use adjusted body weight (ABW) for obese patients [total body weight (TBW) ≥20% of IBW or BMI ≥30 kg/m²]

d) Use total body weight (TBW) if TBW < IBW

Figure 1. Cockroft-Gault Equation

\[
\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{IBW} \times (0.85 \text{ for females})}{\text{SCr} \times 72}
\]

IBW (male) = 50 kg + (2.3 x height in inches > 60 inches)
IBW (female) = 45 kg + (2.3 x height inches > 60 inches)
ABW (kg) = IBW + 0.4 (TBW – IBW)
If ≤65 yo and SCr <1.0 mg/dl → Use SCr = 1.0 mg/dl

2. Loading Doses (see appendix A)

3. Initial Regimen (see appendix B)

B. Dose revisions

1. See Appendix D for calculations
2. Supratherapeutic levels and/or AKI: general approach
a. Do not restart vancomycin until the trough is estimated or confirmed to be at/near the goal trough range. Allow sufficient time for drug clearance before restarting next dose.

b. Actions may include: pre-emptive dose adjustment, holding dose, checking level, discussion with provider, reassessing the need for vancomycin therapy.

c. Consider Scr/renal trajectory when determining next dose and/or level
   i. Ex) rapidly declining Scr may indicate improving renal function warranting earlier redosing vs. rapidly rising Scr indicating ongoing AKI- dose by level may be indicated

C. Monitoring

1. SCr
   a. Upon initiation of the protocol, obtain a STAT SCr if one has not been obtained in the last 24 hours.
   b. Thereafter, order a SCr whenever vancomycin levels are ordered.
   c. For patients with any of the following, ensure SCr is ordered/available x3 days, then PRN:
      i. Rapidly changing renal function
      ii. Critically ill and/or hemodynamically unstable
      iii. Concurrent nephrotoxic agents

2. Trough Levels
   a. Order vancomycin trough levels as appropriate after initiation of therapy and after dose changes.
      i. All levels should be ordered with a SCr except in the case of dialysis patients
   b. Suggested frequency of levels (See Appendix B)
      i. After the target trough level is achieved at steady state, levels should be checked every 3 to 5 days until completion of therapy or discharge.
         a) Levels should be checked sooner when clinically warranted (i.e.: change in clinical status or renal function)
   c. Trough levels are NOT required in the following situations:
      i. One-time dose, followed by cessation of therapy
      ii. Patients on IV vancomycin for <48 hours

3. Adverse Effects
   d. Red Man Syndrome is characterized by hypotension and/or a maculopapular rash appearing on the face, neck, trunk, and/or upper extremities.
   e. If this occurs, pharmacist may slow the infusion rate (e.g. to 90-120 mins per 1 gm.) ± increase the dilution volume upon provider request ± recommend diphenhydramine 25-50mg premedication to the provider

D. Special Populations

1. Dosing by Level
   a. Consider using this strategy in the setting of:
      i. Acute kidney injury (AKI) or acutely fluctuating SCr > 25-50%
      ii. Changing dialysis modes
      iii. Supratherapeutic level

2. Obese: (Refer to Appendix C)

3. Intermittent Hemodialysis (Refer to Appendix E for Algorithms)

4. Continuous Renal Replacement Therapy (Refer to Appendix B)

5. Peritoneal Dialysis (Refer to Appendix B)

C. DOCUMENT INFORMATION
A. Original Author/Date
   Emily Mui, Pharm.D. BCPS: 08/2013

B. Gatekeeper
   Pharmacy Department

C. Distribution
   This procedure is kept in the Pharmacy Policies and Procedure Manual

D. Review/Revision History:
   Lina Meng, Pharm.D., BCPS, BCCCP: 06/2015, 08/2016, 10/2016
   Emily Mui, Pharm.D., BCPS: 08/2016
   Janjri Desai, Pharm.D., MBA, BCPS: 10/2015, 03/2016, 08/2016

E. Approvals
   Antibiotic Subcommittee: 08/2013
   Pharmacy and Therapeutics Committee: 11/2015, 03/2016, 9/2016

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Stanford, CA 94305
APPENDIX A: Loading dose

APPENDIX B: Initial Vancomycin Maintenance Dosing for Non-Obese

APPENDIX C: Vancomycin Dosing in Obesity

APPENDIX D: Dose Revisions

APPENDIX E: Intermittent Hemodialysis Dosing Algorithms

APPENDIX A: Loading dose

I. Purpose:
Ensures (Area Under Curve)/(Minimum Inhibitor Concentration) of >400 mcg-h/mL is achieved on day 1 of therapy for bacterial killing in vitro and clinical outcomes in vivo studies

II. Targeted populations:
- Preferred in seriously ill + suspected/proven severe MRSA infections (e.g. severe sepsis or septic shock, meningitis, endocarditis, MRSA bacteremia)
- All new starts on renal replacement (i.e. IHD, CRRT) should begin with an initial dose of 15-20 mg/kg (exception: PD 10-15mg/kg) regardless of whether they meet the indication above.

III. Standard load for patients with normal renal function: 25-30mg/kg TBW

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Standard Loading Dose ~25 mg/kg TBW</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 – 45 kg</td>
<td>1,000 mg x 1</td>
<td>60 minutes</td>
</tr>
<tr>
<td>46 – 55 kg</td>
<td>1,250 mg x 1</td>
<td>90 minutes</td>
</tr>
<tr>
<td>56 – 65 kg</td>
<td>1,500 mg x 1</td>
<td>90 minutes</td>
</tr>
<tr>
<td>66 – 75 kg</td>
<td>1,750 mg x 1</td>
<td>120 minutes</td>
</tr>
<tr>
<td>76 – 120 kg</td>
<td>2,000 mg x 1</td>
<td>120 minutes</td>
</tr>
<tr>
<td>&gt; 120 kg</td>
<td>2,000 x 1</td>
<td>120-150 minutes</td>
</tr>
</tbody>
</table>

IV. Modified load for special populations: 15-20mg/kg TBW

1. Obese (BMI ≥ 30)
2. CrCl < 30 or AKI
3. IHD, CRRT. PD (10-15mg/kg)
4. Unavailable Scr in emergent situations (e.g code sepsis or ED)

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Modified Loading Dose 15-20 mg/kg TBW</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 – 45 kg</td>
<td>750 mg x 1</td>
<td>60 minutes</td>
</tr>
<tr>
<td>46 – 55 kg</td>
<td>1,000 mg x 1</td>
<td>60 minutes</td>
</tr>
<tr>
<td>56 – 65 kg</td>
<td>1,250 mg x 1</td>
<td>90 minutes</td>
</tr>
<tr>
<td>66 – 75 kg</td>
<td>1,500 mg x 1</td>
<td>90 minutes</td>
</tr>
<tr>
<td>76 – 120 kg</td>
<td>1,750 mg x 1</td>
<td>120 minutes</td>
</tr>
<tr>
<td>&gt; 120 kg</td>
<td>2,000 – 2,500 mg x 1</td>
<td>120-150 minutes</td>
</tr>
</tbody>
</table>

*Time maintenance dose start based on renal function: e.g. wait 24h to start maintenance regimen if CrCl = 30

Use total body weight (TBW); Round doses to nearest 250mg

Peripheral line: max 5mg/mL (including overfill)
Central line only: Up to 1000 mg in 100 mL of compatible diluent

Use total body weight (TBW); Round doses to nearest 250mg

Peripheral line: max 5mg/mL (including overfill)
Central line only: Up to 1000 mg in 100 mL of compatible diluent
**APPENDIX B: Initial Vancomycin Maintenance Dosing for Non-Obese**

I. **Round** doses to nearest 250mg  
II. **Maximum dose**: 2gm in non-obese, IHD, CRRT, PD patients (see Obesity Dosing in Appendix C)

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Dose &amp; Frequency Total body weight (TBW)</th>
<th>TDD Range</th>
<th>Timing Trough Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 90</td>
<td>15 mg/kg Q8H to 15-20mg/kg Q12H</td>
<td>30 – 45 mg/kg/day</td>
<td>Before 4th or 5th dose</td>
</tr>
<tr>
<td>51-89</td>
<td>15 – 20 mg/kg Q12H</td>
<td>30 – 40 mg/kg/day</td>
<td>Before 4th or 5th dose</td>
</tr>
<tr>
<td>30-50</td>
<td>15 mg/kg Q12H to 20 mg/kg Q24H</td>
<td>20 – 30 mg/kg/day</td>
<td>Q12H: before 4th dose Q24H: before 3rd or 4th dose</td>
</tr>
<tr>
<td>10-29</td>
<td>10 – 15 mg/kg Q24H to 15 mg/kg Q48H</td>
<td>7.5 – 15 mg/kg/day</td>
<td>Q24H – before 3rd or 4th dose Q48H – before 2nd dose</td>
</tr>
<tr>
<td>&lt;10 or AKI*, dose by level</td>
<td>15 mg/kg x1, then dose by level</td>
<td>N/A</td>
<td>Within 24 hours of last dose, or with AM labs or every other day</td>
</tr>
</tbody>
</table>

**Hemodialysis**  
- **Initial**: 15 – 20 mg/kg x 1 (max 2gm)  
  - Maintenance: see appendix E  
  - Timing Trough Level: N/A  
  - **Pre-dialysis (preferred)**  
  - **Alternative**: 4 hours after completion of dialysis session

**CRRT†**  
- **Initial**: 15 – 20 mg/kg x 1 (max 2gm)  
  - Maintenance: 10 – 15 mg/kg Q24H  
  - Timing Trough Level: N/A  
  - Before 3rd or 4th dose

**Peritoneal dialysis**  
- 10 – 15 mg/kg x1, then dose by level  
  - Timing Trough Level: N/A  
  - Check level 24h after initial dose. Consult ASP

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*AKI (based on KDIGO, RIFLE, AKIN classifications):*  
i. SCr change by ≥ 0.3 mg/dL within 48h or 50% from baseline or within last 7 days  
ii. CrCl change by >25 - 50%  
iii. Urine output < 0.5 mL/kg/hr over 6 hours (oliguria)

†**Loading and maintenance doses are based on 1-2L/hr dialysate flow and ultrafiltration rates, which is estimated to mimic a creatinine clearance of 30-50 mL/min**

*Ensure SCr available on same days as vancomycin levels*
APPENDIX C: Vancomycin Dosing in Obesity

Major PK alternations in obese populations include increases in Vd, CL, protein binding, and potential shifts to 1-2 compartment models. Analysis by Leong et al in 2011 showed that V_d was increased larger relative to CL, leading to a lower K_el, and subsequently prolonged t½. Lower K_el in obesity may lead to dose "stacking" with Q8H intervals when the dosing frequency τ (tau) approaches t½.

Q8H vs Q12H intervals
- Most studies showed success with Q12H regimens at steady state
- If considering Q8H, reserve for aggressive dosing. Confirm that t½ is < 8 hr!

Calculating BMI
BMI = \text{weight} (kg) / \text{height}^2 (m^2)

Calculating CrCl

<table>
<thead>
<tr>
<th>Weight Category</th>
<th>Definition</th>
<th>Weight to be used for CrCl calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(WHO Class I and II)</td>
<td>BMI 30-40 kg/m²</td>
<td>Adjusted Body Weight IBW + 0.4 (TBW – IBW)</td>
</tr>
<tr>
<td>Extremely obese (WHO Class III)</td>
<td>BMI ≥ 40 kg/m²</td>
<td></td>
</tr>
<tr>
<td>Misc</td>
<td>TBW &gt; 20% above IBW</td>
<td></td>
</tr>
</tbody>
</table>

Calculating t½

<table>
<thead>
<tr>
<th>Step</th>
<th>Equation (adjusted for obese)</th>
<th>Modified CL_vanco</th>
<th>Modified V_d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CL_vanco = CRCl_adjBW x 0.06</td>
<td>BMI ≥ 40 kg/m²</td>
<td>max ~7</td>
</tr>
<tr>
<td>2</td>
<td>V_d = (0.5 – 0.7, see right table) x TBW</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>k = CL_vanco/V_d</td>
<td>BMI 30-40 kg/m²</td>
<td>~0.7 L/kg</td>
</tr>
<tr>
<td>4</td>
<td>t½ = 0.693/k</td>
<td>BMI ≥ 40 kg/m²</td>
<td>0.5 – 0.6 L/kg</td>
</tr>
</tbody>
</table>

Initial Dosing

<table>
<thead>
<tr>
<th>Loading Dose</th>
<th>Indication</th>
<th>Initial 24 hr max (Load + Maintenance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 - 20 mg/kg TBW (max 2,500 mg)</td>
<td>Rapid attainment of initial trough &gt; 15 in severely ill + severe sepsis, septic shock, suspected/proven MRSA bacteremia, MRSA meningitis or MRSA endocarditis</td>
<td>4.5 grams</td>
</tr>
</tbody>
</table>

Initial Maintenance Dose for CrCl > 60 mL/min

<table>
<thead>
<tr>
<th>BMI</th>
<th>Dosing Regimen</th>
<th>Total Daily Dose (TDD)</th>
<th>Timing Trough Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>10 – 15 mg/kg TBW (max 2g) Q12H*</td>
<td>20 – 30 mg/kg/day</td>
<td>Initial check: before 4th-5th dose (including load) or earlier if suspect supra-therapeutic level or if rise in SCr &gt; 25%</td>
</tr>
<tr>
<td>≥ 40</td>
<td>7.5 – 12.5 mg/kg TBW (max 2g) Q12H*</td>
<td>15 – 25 mg/kg/day</td>
<td>Subsequent levels: 2nd level 24-48h after 1st level, if in range and SCr stable, may space out Q3 -5 days</td>
</tr>
</tbody>
</table>

* Note: For those with CRCL_adjBW > 120mL/min, Q8H may be considered if t½ < 8hr. Convert the TDD above to Q8H (max 4.5g/day) ± 10 mg/kg initial dose if no load given/indicated.
APPENDIX D: Dose Revisions

1. **PK calculator**: After the first trough level results, may calculate subsequent dose regimens using revision kinetics assuming stable renal function and steady state conditions.

   See [SHC Vancomycin PK Guide](#)

2. **Linear proportion method**: Assuming linear PK, changes to TDD have a corresponding proportional change in troughs when maintaining the same dosing interval, assuming stable renal function and steady state conditions.

   \[
   \frac{C_{\text{min (observed)}}}{C_{\text{min (desired)}}} = \frac{\text{Current TDD}}{\text{New TDD}}
   \]

   E.g.: 1000mg IV Q12H results in a trough of 10. To target a trough of 15, you would target a 50% increase in TDD.

   \[
   \text{New TDD} = \frac{15 \times 2000 \text{mg}}{10} = 3000 \text{ mg}
   \]

   Your calculated new TDD comes out to 3000 mg. You can give this as 1500mg Q12H, or if the patient’s half life is < 8 hours, consider a Q8H regimen. **Note**: maintaining the same TDD but dividing it Q8H will result in a non-linear increase in trough. E.g. Expect a trough higher than 15 with 1000mg Q8H.
APPENDIX E: Intermittent Hemodialysis Dosing Algorithms

For goal trough 10-15 mcg/ml:

1. **Goal trough 10-15**
   - Vancomycin Loading Dose 15mg/kg (max 2000mg)

2. **1st HD session**

3. **Draw pre-HD level before next HD session**
   - (e.g. AM labs of 2nd HD session)

   - Pre-HD level 5-10: give 500-1000 mg or 7.5-10mg/kg post HD
   - Pre-HD level 10-15: give 250-500mg or 5 mg/kg post HD
   - Pre-HD level 15-20: give 250 mg or 2.5 mg/kg post HD
   - Pre-HD level > 20: HOLD vancomycin until level back in range

4. **Repeat algorithm based on level prior to next HD session**

- Assumes 1) anuric 2) that HD is high flux and removes ~20% of vancomycin per 3 hour HD session
- If pre-HD level severely subtherapeutic, consider dosing pre-HD (instead of post-HD), but boost the recommended dose by 20% depending on acuity/severity of infection and potential harm/risk from underdosing while awaiting dialysis completion.
For goal trough 15-20 mcg/ml:

Goal trough 15-20 mg/dl
Vancomycin Initial Dose
15-20mg/kg (max 2000mg)

1st HD session

Draw pre-HD level before next HD session
(e.g. AM labs of 2nd HD session)

Pre-HD level < 10:
give 10-15mg/kg post HD

Pre-HD level 10-15:
give 500-1000 mg or 7.5-10mg/kg post HD

Pre-HD level 15-20:
give 250-500mg or 5 mg/kg post HD

Pre-HD level 20-25:
give 250 mg or 2.5 mg/kg post HD

Pre-HD level > 25:
hold vancomycin until level back in range

Repeat algorithm based on level prior to next HD session

- Assumes 1) anuric 2) that HD is high flux and removes ~20% of vancomycin per 3 hour HD session
- If pre-HD level severely subtherapeutic, consider dosing pre-HD (instead of post-HD, but boost the recommended dose by 20%) depending on acuity/severity of infection and potential harm/risk from underdosing while awaiting dialysis completion.
REFERENCES

11. Winter, Michael E., Basic Clinical Pharmacokinetics, 5th ed, Lippincott Williams & Wilkins

Obesity references: