IMPROVING VANCOMYCIN DOSING AND MONITORING IN THE ABSENCE OF A FORMAL PHARMACOKINETIC SERVICE:

IMPACT OF A PHARMACY DEPARTMENT-WIDE APPROACH IN A COMMUNITY HOSPITAL SETTING

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Guideline Summary of Recommendations:

- "It is recommended that trough serum vancomycin concentrations always be maintained above 10 mcg/mL to avoid development of resistance"

- "Trough serum vancomycin concentrations of 15-20 mcg/mL are recommended"… troughs “in that range should achieve an AUC/MIC of ≥400 in most patients if the MIC is ≤1 mcg/mL”

- “A targeted AUC/MIC of ≥400 is not achievable with conventional dosing methods if the vancomycin MIC is ≥2 mcg/mL in a patient with normal renal function”…”alternative therapies should be considered”
Vancomycin Dosing Guidelines 2009

- Guideline Summary of Recommendations:
  - **Loading Doses:** “In order to achieve rapid attainment of the target concentration for seriously ill patients, a loading dose of 25-30 mg/kg should be considered”
    - Bacteremia, endocarditis, osteomyelitis, meningitis, HAP
  - **Maintenance Doses:** “Dosages of 15-20 mg/kg given every 8-12hrs are required for most patients with normal renal function”

- Following these recommendations can be challenging:
  - Many physicians still reluctant to use such high doses
  - Many hospitals implement formal pharmacokinetic service
    - Staffed by clinical specialist with help/coverage from pharmacy residents
  - Some hospitals rely on decentralized pharmacists to monitor during daily patient reviews (but not all patients are reviewed / followed)
    - Evening and overnight issues are left for the following day
Process for Change

- Are we following the vancomycin dosing guidelines?
  - Complete an assessment of vancomycin dosing before any changes

- Create a new order set “PowerPlan” in Cerner for vancomycin using a mg/kg dosing strategy

- Educate the pharmacists on the dosing guidelines
  - Vancomycin presentation / CE competency
  - Vancomycin monitoring worksheet (quality-control measure)

- Obtain P&T approval for new dosing plan and pharmacist weight-based dosing policy

- Educate Cerner prescribers on new PowerPlans

- Did we improve?
  - Complete an assessment after the changes
Identifying the Problem

• May 2012: preliminary data on 100 patients showed:
  • Only 52% were prescribed correct initial vancomycin dose per 2009 ASHP/IDSA guidelines
  • Only 24% had an initial trough at goal
  • 48% had an initial trough <10 mcg/mL

• Order sets were developed that require weight-based vancomycin dosing through Cerner
  • Live in Cerner since 2/15/13
  • Pharmacist weight-based dosing policy approved to allow pharmacist to apply the appropriate weight to a mg/kg dose and round to the nearest 250mg
    • Policy also allows a pharmacist to enter/cancel vancomycin levels/ troughs when appropriate per protocol
Vancomycin Initial (CrCl >30/not on HD):

DOSING RECOMMENDATIONS:
- Use a 20 mg/kg loading dose for mild infections, e.g., cellulitis (negative blood cultures)
- Use a 25 mg/kg loading dose for serious infections, e.g., hospital acquired pneumonia
- Use a 30 mg/kg loading dose for e.g., meningitis, endocarditis or osteomyelitis
- For obese patients, consider a loading dose of 25-30 mg/kg

Choose 20 mg/kg “once” if patient does not require a loading dose

Maintenance Dose:

DOSING RECOMMENDATIONS:
- For patients <45 y/o and CrCl >100, dose vancomycin every 8 hours
- For patients with CrCl 50-100, dose vancomycin every 12 hours
- For patients with CrCl 30-49, dose vancomycin every 24 hours

Maintenance dose will be automatically timed 8, 12 or 24 hours after the first dose

Please order a BUN and Creatinine ONLY if a BMP is NOT ordered

BUN

Creatinine

Blood, Routine collect, daily
Vancomycin Order Sets

This order will place a “marker” that stays on the med profile alerting clinicians that the patient is receiving one-time doses of vancomycin.
In addition, pharmacists were trained to use a monitoring tool for both initial dosing and daily monitoring

- Every patient started on vancomycin has a monitoring form started regardless of shift and including weekends → this is completed automatically without an order for “pharmacy consult”

- Day shift pharmacists are responsible for completing the daily assessment to determine if changes to scheduled doses or levels need to be made (monitoring sheets are kept in folders according to day-shift pharmacist floor assignments)

- Level results print directly to pharmacy in real-time and pharmacists on all shifts follow-up with dose change recommendations and schedule subsequent levels

- All dose changes are still discussed with physicians, although some physicians do write orders such as “pharmacy to dose subsequent vancomycin orders”
# Vancomycin Monitoring Form

**Date/Time form started:** / / @

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>FIN:</th>
<th>Age: yrs</th>
<th>Gender: M F</th>
<th>Hr: in</th>
</tr>
</thead>
<tbody>
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</table>

**Antibiotic Allergies:**
- Omeprazole (Bactrim)
- Quinupristin-dalfopristin (Staphylococcus aureus)
- Tetracycline (Staphylococcus epidermidis)
- Macrolide (Campylobacter jejuni)
- Penicillin (treated or not in the past or non-penicillinase-producing) (treatment or non-treatment may be allergic response) (antibiotics other than penicillin or non-penicillinase-producing) (treatment or non-treatment may be allergic response) (other antibiotic allergies)

**Location when ordered:**
- ER, PACU, ICU, 3W, CCU, IMC, N3S, PCU, 4W, 4NW, 4S, 5W

## Initial Patient Characteristics

**Weights:**
- Ideal Body Weight (IBW): kg
- Total Body Weight (TBW): kg
- Adjusted Dosing Weight (ADW): kg

**Scr:** mg/dL

**CrCl:** mL/min calculated as:
- IBW = TBW (if IBW = TBW) or ADW (if IBW not ≥75% above TBW)

## Indication for Vancomycin

(This can be filled out on day 2 once an InP is available)

**Loading Dose Recommended:**
- Pneumonia (empyema/MRSA suspected)
- Pneumonia (MRSA in culture)
- Bacteremia (Gram +/coli/MSA in culture)
- Endocarditis (proven or suspected)
- Osteomyelitis (proven or suspected)
- Abscess (deep tissue infection, associated with poor vascular blood flow)
- Sinusitis (infection of the sinus cavity)
- Other:

**Loading Dose may be used but not necessary:**
- If vancomycin MIC is known and the goal trough is 15-20 mg/mL, the goal trough is 10-15 mg/mL regardless of indications
- Consider LD in obesity regardless of indication

## Vancomycin Orders

**Prescriber:**

**Use TBW for dosing if TBW ≥75% above IBW use ADW

**Follow this section only if vanco was not ordered through a powerplan:**

**Prescriber Ordered Loading Dose:**
- mg IV once (max 2000 mg)

**RPS Calculated Loading Dose:**
- mg IV once.

**Prescribed Order Maintenance Dose:**
- mg IV Q time or once (max 2000 mg/dose)

**Prescriber Ordered Maintenance Dose:**
- mg IV Q time or once (max 2000 mg/dose)

## Ccr

**Interval:**
- ≥ 30
- 15-30
- <15

## Flowchart:

- N = Reason
- Y = New dose recommended
- N = Prescriber contacted
- Y = Prescriber contacted

## Monitoring:

**Actual time adjusted dose:** (see “MAP Summary” tab or “MAP” window, write “held” if dose not given)

**Goal trough:** specified by prescriber
- Y = mg/mL
- N = RPH specifies trough of

**ER Dose or Loading Dose:**
- mg Date/Time: / / @

**Partial doses (e.g., extra 50 mg to make up loading dose 1500 mg if only 1 mg given in ER):**
- mg Date/Time: / / @

**Total First Dose:**
- mg

<table>
<thead>
<tr>
<th>Date</th>
<th>Dose (mg)</th>
<th>Int. (h)</th>
<th>Level</th>
<th>Other Labs</th>
<th>Pharmacist Notes / Interventions / New Stain Results (eg. MSA gave change from to antibiotics)</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>

- Y = Level needed to continue
- N = Level needed to continue
- **SCR:** WBC
- **CR:** T 37.5°C
## VANCOMYCIN MONITORING FORM

**RPh Initiating Form:** (initials)  
**Date/Time form started:** __/__/__ @ __:__

**Patient Name:** ___________________  
**FIN:** ____________  
**Age:** __________ yrs  
**Gender:** □ M  □ F  
**Ht:** __________ in.

**Antibiotic Allergies:**  
- □ none  
- □ sulfa (Bactrim)  
- □ quinolone  
- □ tetracycline  
- □ macrolide  
- □ penicillin (tolerated ceph. in past or non-anaphylaxis)  
- □ other: ___________________  
- □ penicillin (ceph. not tolerated or not in med. history or anaphylaxis)

**Location when ordered (circle):**  
- ER  
- PACU  
- ICU  
- 2W  
- CCU  
- IMC  
- 3N  
- 3S  
- PCU  
- 4W  
- 4N  
- 4NW  
- 4S  
- 5W

### INITIAL PATIENT CHARACTERISTICS (at the time vancomycin is ordered):

**Weights:**  
- Ideal Body Weight (IBW): _______ kg  
- Total Body Weight (TBW): _______ kg  
  - □ ≥25% above IBW? □ Y  □ N  
  - if yes, calculate ADW below  
- Adjusted Dosing Weight (ADW): _______ kg  
  - ADW = 0.4 (TBW - IBW) + IBW  
  - □ N/A (TBW not ≥25% above IBW)

**SCr:** ____ mg/dL  
**CrCl:** ____ mL/min  
- calculated with: □ IBW  □ TBW (if < IBW)  □ ADW (if TBW ≥25% above IBW)

### INDICATION FOR VANCOMYCIN:  
(This can be filled out on day 2 once an H&P is available)

**Loading Dose Recommended (goal troughs 15-20 mcg/mL)***:  
- □ Pneumonia (empiric/MRSA suspected)  
- □ Pneumonia (MRSA in cultures)  
- □ Endocarditis (proven or suspected)  
- □ Meningitis (proven or suspected)  
- □ Abscess/Deep tissue infection (ie: diabetic foot w/poor vascular bloodflow)  
- □ MRSA in culture not listed above  
  - → site of infection: ___________________
  - □ Bacteremia (Gram + cocci/ MRSA in cultures)  
  - □ Osteomyelitis (proven or suspected)  
  - □ Severe sepsis (unknown source)  
  - □ Other: ___________________

**Loading Dose may be used but not necessary*** (goal troughs 10-20 mcg/mL):  
- □ Mild cellulitis (with negative blood cultures)  
- □ UTI (with negative blood cultures)  
- □ Not reported

**Vancomycin MIC** _______ mcg/mL  
- □ Not reported

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*If vancomycin MIC is known and is ≥ 1 mcg/mL the goal trough = 15-20 mcg/mL regardless of indication

**Consider LD in obesity regardless of indication**
VANCOMYCIN ORDERS:  Prescriber:  
*Use TBW for dosing if TBW ≥25% above IBW use ADW

☐ Ordered through Vanco Initial (CrCl >30, not on HD) PowerPlan (skip below calculations)  
☐ Active order placeholder entered
  □ Trough lab order is entered
  □ Intervention opened (leave open)

☐ Ordered through Vanco Initial (CrCl <30 or on HD) PowerPlan (skip below calculations)

☐ Trough lab order is entered

FILL OUT THIS SECTION ONLY IF VANCO WAS NOT ORDERED THROUGH A POWERPLAN:

Prescriber Ordered LOADING Dose: ______ mg IV once (max 2000 mg)  
  □ Not ordered  
  □ Active order placeholder entered
  □ Trough lab order is entered
  □ Intervention opened (leave open)

RPh calculated loading dose: 25 mg/kg = ______ mg

Wt used:  
  □ TBW ___ kg  
  □ ADW ___ kg

Does ordered dose fall within this range?  
  □ Y  
  □ N  
  □ New dose recommended: ______ mg IV once
  □ New dose accepted?  
  □ Y  
  □ N

Prescriber Ordered MAINTENANCE Dose: ______ mg IV Q ______ hrs or □ once (max 2000 mg per dose)

RPh calculated maint. dose: 15 mg/kg = ______ mg

Wt used:  
  □ TBW ___ kg  
  □ ADW ___ kg

Does ordered dose fall within this range?  
  □ Y  
  □ N  
  □ New dose recommended: ______ mg IV Q ______ hrs
  □ New dose accepted?  
  □ Y  
  □ N

□ CrCl <30 mL/min  
  □ One-time dose by levels ordered
  □ Active order placeholder entered

□ Hemodialysis  
  □ One-time dose by levels ordered
  □ Trough lab order is entered

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Interval</th>
</tr>
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<tbody>
<tr>
<td>≥ 50</td>
<td>Q8-12hrs (Q8hr interval often needed for patients age 20’s – 50’s with CrCl &gt;100 mL/min)</td>
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<tr>
<td>30-49</td>
<td>Q24hrs</td>
</tr>
<tr>
<td>15-29</td>
<td>Q48hrs but recommend dose by levels</td>
</tr>
<tr>
<td>&lt;15</td>
<td>Q48-72hrs but recommend dose by levels</td>
</tr>
<tr>
<td>Dialysis</td>
<td>Re-dose when level falls below goal trough</td>
</tr>
</tbody>
</table>

Re-dosing by levels:
  If level 10-20 give 15mg/kg once
  If level 5-9 give 20mg/kg once
  If level ≤5 give 25mg/kg once

MONITORING:  *Actual time nurse administered dose (see “MAR Summary” tab or “eMAR”; write “held” if dose not given)

TO BE FILLED OUT ON DAY SHIFT FOR EVERY PATIENT (including those with open intervention), INCLUDING WEEKENDS.  2nd and 3rd SHIFT COMPLETES PENDING LEVELS DURING THAT SHIFT, THEN PLACES BACK IN DAY SHIFT FOLDER.

Goal trough specified by prescriber?  
  □ Y  
  □ N  
  □ Correct goal based on above indications?  
  □ Y  
  □ N  
  □ RPh specifies trough level

□ N  
  □ RPh specifies goal trough of ______ mcg/mL for monitoring purposes

ER Dose or Loading Dose given: ______ mg Date/Time: / / / @:  
  □ N/A

Partial doses (ie. extra 500mg to make up loading dose 1500 mg if only 1gm given in ER): ______ mg Date/Time: / / / @:  

Total First Dose: ______ mg
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<td>Does vanco need to continue?</td>
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<td></td>
<td>Y       N</td>
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<td></td>
<td>Level pending: / / @ :</td>
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<th>Actual* Admin. Times:</th>
<th>Time drawn:</th>
<th>Level: →  hr level</th>
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<td>Y       N</td>
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</table>

SCr:  
WBC:  
- Afebrile 
- T > 37.9 C 
- Drugs that 
  - ↑Vd or Clearance 
  - Pressors 
  - Diuretics 
  - Fluids high volume 

RPh:
Baseline Characteristics

- Data collected on all initial vancomycin starts in a 30 day period: March 25-April 23, 2013 (~ 1 month after PowerPlan go-live)

<table>
<thead>
<tr>
<th>Total Number of Patients</th>
<th>154</th>
</tr>
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<tbody>
<tr>
<td><strong>Age (years):</strong></td>
<td></td>
</tr>
<tr>
<td>18-59</td>
<td>29%</td>
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<tr>
<td>60-79</td>
<td>43%</td>
</tr>
<tr>
<td>&gt;80</td>
<td>29%</td>
</tr>
<tr>
<td><strong>CrCl (mL/min)</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;50</td>
<td>51%</td>
</tr>
<tr>
<td>30-49</td>
<td>25%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>24%</td>
</tr>
</tbody>
</table>

* Age <60 yrs and CrCl >100mL/min (13% of total vancomycin orders)
** HD patients account for 8% of total vancomycin orders
Initial Dose Outcomes
Loading Doses

Pre- and Post- Change Loading Dose Comparison

- Loading Dose Indicated: 84% Pre-Change, 89% Post-Change
  - p = 0.258

- LD Ordered if Indicated: 3% Pre-Change, 74% Post-Change
  - p = <0.0001

- Ordered LD was 25-30 mg/kg: 0% Pre-Change, 84% Post-Change
  - p = <0.0001

67% ordered through PowerPlan
Maintenance Doses

Pre- and Post-Change Maintenance Dose Comparison

Ordered Maintenance Dose was 15-20 mg/kg
Ordered Interval was Correct
Initial Dose and Interval Correct

66% 86% 52%
72% 84% 71%

$p = <0.0001$ $p = 0.0275$ $p = 0.0021$

56% ordered through PowerPlan
Initial Dose Outcomes Summary

Through the use of new dosing PowerPlans and greater pharmacist involvement we have seen statistically significant increases in:

- The correct use of loading doses
- The number of patients with a correct initial guideline-based dosing regimen
- Pharmacist interventions: dosing recommendations have a high acceptance rate
Initial Level and Monitoring Outcomes
133 initial levels were available in the Post-Change group
Initial Levels

Pre- and Post- Change Total Initial Level Comparison

- **Level Too Low**
  - Pre-Change: 68%
  - Post-Change: 33%
  - $p = < 0.0001$

- **Level <10**
  - Pre-Change: 48%
  - Post-Change: 16%
  - $p = < 0.0001$

- **Level Too High**
  - Pre-Change: 7%
  - Post-Change: 16%
  - $p = 0.0793$
Monitoring and Dose Adjustments During Therapy: Pharmacist Involvement

![Bar chart showing pre- and post-change pharmacist monitoring comparison.](chart.png)

Pre- and Post-Change Pharmacist Monitoring Comparison

Pharmacist intervened when necessary during monitoring of levels.

<table>
<thead>
<tr>
<th>Pre-Change</th>
<th>Post-Change</th>
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<tbody>
<tr>
<td>42%</td>
<td>94%</td>
</tr>
</tbody>
</table>

$p = <0.0001$
### “High” Levels

<table>
<thead>
<tr>
<th>Level too high at some point in therapy</th>
<th>31</th>
<th>23%</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 were a high initial level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 (8%) patients had high levels during the monitoring / dose adjustment process</td>
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</tr>
</tbody>
</table>

#### Range of High Levels (mcg/mL)
- 20-30: 84%
- 31-40: 19%
- >40: 3%

#### Age Range of High Level Patients (years)
- 18-59: 32%
- 60-79: 52%
- >80: 16%
Initial “High” Levels

Possible Reasons for High Level

- SCr increased during therapy: 42%
- Unknown / Unexplained: 26%
- Incorrect Initial Dose: 16%
- Dose accumulation (>5-7 days of therapy): 10%
- Physician did not follow pharmacist's recommendation: 3%
- Scheduled dose instead of dose by levels: 3%
- Scheduled dose instead of dose by levels: 3%
- Scheduled dose instead of dose by levels: 3%
Level and Monitoring Outcomes: Summary

- Through the use of new dosing computerized order sets and greater pharmacist involvement we have seen statistically significant increases in:
  - Initial levels ordered within the correct timeframe
  - The initial levels that are at goal \textit{without} a statistically significant increase in levels that are \textit{too high}
  - Pharmacist interventions for dose adjustments during monitoring

- And statistically significant decreases in:
  - Initial levels that are too low
  - Initial levels $<$10 mcg/mL

- No major safety hazards were identified with the new dosing strategy or order sets
  - Nephrotoxicity was not higher than what is reported in literature