Laguna Honda Hospital Adult Intravenous Vancomycin Per-Pharmacy Dosing Protocol

PURPOSE:
To establish a framework for pharmacist-directed management of IV vancomycin therapy in adult patients which includes initial dosing, monitoring of pertinent laboratory values and vancomycin levels, and dose modification. Other institutions with similar pharmacist-led dosing protocols have shown optimized outcomes, such as higher proportions of vancomycin trough levels within therapeutic range.

POLICY:
To establish a standardized protocol for vancomycin dosing and monitoring in adult patients intended to optimize efficacy and reduce the potential for adverse events. Based on this protocol, pharmacists will be able to write orders for vancomycin dose, trough levels, and related laboratory studies as specified. See below for inclusion and exclusion criteria.

ORGANIZATION:
The clinical pharmacist will coordinate the vancomycin service and will determine patient-specific intervals for lab draws, evaluate patient's vancomycin therapy, and make dosage adjustments per protocol if necessary. The pharmacist will be available to evaluate all vancomycin levels and related monitoring labs returning between the hours of 8am-4:30pm on Monday-Friday. All other lab results which return outside this designated window must be evaluated and acted upon by the primary or covering physician. The physician will provide information regarding interventions and blood draw intervals to the clinical pharmacist when they are next available.

When outlined by the protocol, or at any time an unusual or unexpected situation arises, the clinical pharmacist will consult the primary or covering provider for medical guidance. If the patient has a critically high lab value related to vancomycin monitoring as indicated by the protocol, then appropriate interventions will be initiated after discussion with the physician. If adverse reaction is noted, the primary or covering physician and the clinical pharmacist will be notified and the corresponding physician will evaluate the patient for appropriate management.

DEFINITIONS:
Setting/Patient Population
1. Inclusion Criteria:
All adult patients admitted to LHH receiving IV vancomycin therapy. Note: Physicians are able to opt out of the pharmacist-driven protocol and order vancomycin doses and levels independently.

2. Exclusion Criteria:
This protocol is not intended for the scenarios below:

a. Patients whose physician has opted out of the pharmacist-driven protocol.
b. Patients initiated on IV vancomycin for anticipated duration < 24 hours including single dose or for peri-operative prophylaxis use.

PROCEDURES:

1. **Pharmacist-managed IV vancomycin management protocol:**
   a. **Initiation and Discontinuation of the protocol**
      i. Physician orders IV vancomycin per pharmacy and specifies the indication, duration and goal trough levels.
         1. Physicians will leave all dosing decisions to pharmacist discretion by ordering the consult order, "Pharmacy consult – dose vancomycin". The pharmacist may adjust any loading and maintenance doses placed by the physician, if appropriate.
         2. Physicians may opt-out and manage all doses and levels, as described above.

      ii. Pharmacists will be responsible for initiating, evaluating, and/or modifying vancomycin dosing regimen and laboratory values for any patients with the pharmacy consult order.

      iii. Physicians who order vancomycin per pharmacy consult may discontinue and/or reinitiate the protocol at any time.

      iv. Upon receiving orders to discontinue therapy, pharmacists will ensure all related orders are discontinued (e.g. labs, trough level, med order, and consult order). If there is any uncertainty about whether the per pharmacy protocol should be discontinued, the pharmacist will contact the physician for clarification.

   b. **IV Vancomycin Regimen Management**
      i. Upon receipt of a vancomycin per pharmacy consult order, pharmacists will order the initial IV vancomycin regimen if not done by physician or assess the appropriateness of the initial IV vancomycin regimen ordered by the physician based on patient-specific parameters (e.g., height, weight, renal function, indication, pharmacokinetic goal).

      ii. Pharmacists may adjust an existing vancomycin order, as clinically appropriate, once the protocol is active.

      iii. The pharmacist will be responsible for ordering and timing vancomycin trough and/or random level(s) and adjusting regimens, as appropriate.

      iv. Dose and/or frequency adjustments by pharmacists will be based on the UCSF Antimicrobial Dosing Guidelines, the vancomycin dosing nomogram, and pharmacokinetic analysis. (See Appendix A for details).

      v. Modifications to IV Vancomycin therapy by the pharmacist will be documented in the notes section of the electronic medical record (EMR).

   c. **IV Vancomycin Level Monitoring**
      i. After initiation of the protocol, pharmacists will order or adjust the timing of vancomycin levels according to protocol. In addition to vancomycin levels, pharmacists are authorized to order laboratory values necessary to evaluate the safety and efficacy of IV vancomycin, including, but not limited to:
         1. Serum creatinine (SCr)

a. If no baseline SCr is available, pharmacists should order one "STAT". When treating serious infections, it is reasonable to proceed with an initial dose prior to the SCr result.
b. SCr should be ordered daily for acute care patients receiving IV vancomycin; pharmacists can place orders if not otherwise followed by physicians.
c. Long term care patients will have SCr checked weekly or as appropriate

2. Blood urea nitrogen (BUN)
   a. BUN can be followed weekly; pharmacists can place orders if not otherwise followed by physicians.
3. CBC with differential
   a. CBC can be followed weekly; pharmacists can place orders if not otherwise followed by physicians.
   b. CBC with differential should be ordered daily for acute care patients

ii. Pharmacists will be available to review or provide guidance on vancomycin dosing based on levels and renal function regardless of protocol status. If a per pharmacy consult order has not been placed, this indicates the physician will manage vancomycin dosing and monitoring. In these cases, pharmacists will communicate recommendations to physicians rather than make changes independently.

iii. Goal trough level (Table 1)
If monitoring AUCs, the goal will generally be 400 – 600 mg*hr/L. If monitoring trough levels, the goal will be as follows:

Table 1. Goal Trough Level by Indication

Indication	Goal Trough (mg/L)
Skin/Soft tissue infections, UTI	10-15
Bacteremia, Endocarditis, Meningitis, Pneumonia, Severe Sepsis, Osteomyelitis, Hardware Infections, Febrile neutropenia or other serious infections not listed above	15-20

iv. If the vancomycin trough is above goal or if there are any concerns while on IV vancomycin, the pharmacist will check in with the nurse for potential side effects. The physicians will be notified of any of the following:
1. Any new onset of rash (e.g. maculopapular rash vs. vancomycin flushing syndrome)
2. Ototoxicity (e.g. hearing loss, tinnitus)
3. Infusion site reactions (e.g. phlebitis, pruritus, irritation, pain)
4. Hypersensitivity reactions or anaphylaxis during and after the infusion (e.g. fever, dyspnea, wheezing, chest pain, hypotension)

d. Regimen adjustments for Vancomycin

i. The pharmacist will use the vancomycin dosing nomogram, the guidance for dose modification, and pharmacokinetic calculations (Appendix A) to determine the optimal dose of IV vancomycin for the patient. These references do not replace clinical judgment.

ii. The pharmacist may consult with the ID physician if necessary.

iii. Pharmacists may temporarily discontinue IV vancomycin for supratherapeutic vancomycin levels and re-order vancomycin therapy regimen when levels have returned to goal range, as clinically appropriate.

e. Vancomycin Duration

i. The physician is responsible for determining duration of IV vancomycin therapy. The pharmacist will evaluate need for ongoing IV vancomycin therapy and may recommend discontinuation of vancomycin therapy or request review by antimicrobial stewardship team member.

ii. When a physician discontinues the IV vancomycin order, pharmacists are authorized to discontinue the protocol and associated lab orders.

2. DOCUMENTATION

a. Pharmacists will place an order in the electronic medical record (EMR) for initial IV vancomycin doses, dose or frequency modifications, or laboratory values.

b. Pharmacists will document rationale for all vancomycin regimens (initial or modifications) and pharmacokinetic assessments in a note in the EMR.

3. TRAINING

a. Pharmacists will undergo clinical training and must be credentialed by medical staff every 2 years in order to provide services under the protocol.

b. The credentialing process will be managed by the medical executive committee.

4. QUALITY ASSURANCE

a. The Pharmacy Department at LHH will have oversight of the pharmacist managed IV vancomycin protocol.

b. The clinical pharmacist team will ensure regular review of the protocol, working in collaboration with the Interdisciplinary Practices Committee, the Antimicrobial Stewardship Program and Laboratory Medicine.

c. Data describing program outcomes will be presented to the Pharmacy & Therapeutics Subcommittee (LHH), Antimicrobial Stewardship Program (LHH), and Antibiotic Subcommittee (ZSFG) periodically.

ATTACHMENT:

Appendix A: **Clinical Guidance for Adult IV Vancomycin Per-Pharmacy Dosing Protocol**

REFERENCES:

1. Adapted from ZSFG Adult Intravenous Vancomycin Per-Pharmacy Dosing Protocol.
2. Crew P, Heintz, S, Heintz, B. Vancomycin dosing and monitoring for patients with end-stage renal disease receiving intermittent hemodialysis. Am J Health-Syst Pharm. 2015;72:1856-1864.
3. Heintz B, et al. Antimicrobial dosing concepts and recommendations for critically ill adult patients receiving continuous renal replacement therapy or intermittent hemodialysis. Pharmacotherapy. 2009;29(5)562-577.
4. Infectious Diseases Management Program. 2014. http://idmp.ucsf.edu (Accessed October 2018).
5. Kullar R, Davis SL, Levine DP. Impact of Vancomycin Exposure on Outcomes in Patients With Methicillin-Resistant Staphylococcus aureus Bacteremia: Support for Consensus Guidelines Suggested Targets Clinical Infectious Diseases 2011;52(8):975–981.
6. Levin D, Glasheen JJ, Kiser TH. Pharmacist and Physician Collaborative Practice Model Improves Vancomycin Dosing in an Intensive Care Unit. International Journal of Clinical Medicine 2016; 7:675-685.
7. Levin D, Kiser TH. Evaluation of a multidisciplinary intervention on initial vancomycin dosing in the intensive care unit. American College of Clinical Pharmacy Spring Meeting. Charlotte, North Carolina. Pharmacotherapy 2010;30(4):162e Abstract 37E
8. Levin D, Kiser TH, Pell J, Glasheen JJ. Inadequate Initial Vancomycin Dosing in an Intensive Care Unit. Society of Hospital Medicine Meeting. Chicago, Illinois. May 2009
9. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, Kaplan SL, Karchmer AW, Levine DP, Murray BE, M JR, Talan DA, Chambers HF. 2011. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: executive summary. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America 52:285-292.
10. Rybak M et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists; Am J Health-Syst Pharm. 2020;77:835-64.
11. Rybak M, et al. Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Disease Society of American and the Society of Infectious Disease Pharmacists; Am J Health-Syst Pharm. 2009;66:82-98.
12. Winter ME. 2010. Basic clinical pharmacokinetics, 5th ed. Wolters Kluwer/Lippincott Williams & Wilkins Health, Philadelphia.

Appendix A:

Clinical Guidance for Adult IV Vancomycin Per-Pharmacy Dosing Protocol

1. Gather pertinent info
    a. Patient Specific
        i. Age
        ii. Sex
        iii. Height
        iv. Weight
        v. Serum creatinine (most recent and trend)
        vi. Renal replacement therapy (hemodialysis, CRRT, peritoneal dialysis)
        vii. Allergies
        viii. Pregnancy status
        ix. Hemodynamic status (BP, HR, RR, temp)
    b. Infection Specific
        i. Indication, Goal Trough Level

Table 1: Goal Trough Levels

Indication	**Goal Trough (mg/L)**
Skin/Soft tissue infections, UTI	10-15
Bacteremia, Endocarditis, Meningitis, Pneumonia, Severe Sepsis, Osteomyelitis, Hardware Infections, Febrile neutropenia, or other serious infections not listed above	15-20

Note: if monitoring AUCs, the goal will generally be 400 – 600 mg*hr/L.

        ii. Determine whether this is a new start or dose modification
            1. Review current/ historic med list for prior vancomycin dose
            2. Review patient chart for prior vancomycin levels, SCr
        iii. If applicable, review appropriateness of prior vancomycin levels
            1. Drawn at steady state?
                a. Usually defined as a level drawn just prior to the 4th or 5th dose
            2. Drawn at the appropriate time?
                a. E.g. a true trough is drawn approximately 8 hours *after* prior dose when scheduled Q8h or 12 hours *after* prior dose when scheduled Q12h, etc.

2. Calculate estimated creatinine clearance (CrCL)
    a. Use Cockcroft-Gault equation

$$\frac{(140 - \text{age}) * \text{weight}}{} \quad (*0.85 \text{ if female})$$

72 * SCr

i. Use IBW to calculate estimated CrCL for most patients

IBW (male) = 50 kg + 0.91 * (cm > 152 cm)

IBW (female) = 45.5 kg + 0.91 * (cm >152 cm)

ii. Use Adjusted BW (if TBW >120% of IBW)

Adjusted BW = IBW + 0.4 * (actual BW – IBW)

iii. Use TBW if TBW < IBW
iv. Consider round up SCr to 0.7 mg/dL if < 0.7 mg/dL
v. Keep in mind this equation may underestimate CrCl if SCr is improving or overestimate CrCl if SCr is worsening; SCr trends must be considered when evaluating appropriate doses

3. Calculate Initial Loading Dose
    a. Appropriate for most patients with a complicated infection (e.g. goal 15-20 mg/L)
        i. Critical illness requiring vasopressors
        ii. Bacteremia
        iii. Endocarditis
        iv. CNS infections (e.g. meningitis)
        v. Pneumonia
        vi. Severe sepsis or septic shock
        vii. Osteomyelitis
    b. Vancomycin 20-25 mg/kg IV x1
        i. Based on **total BW**
        ii. Round to nearest 250 mg
        iii. Maximum 2 g dose

4. Calculate Initial Maintenance Dose
    a. Recommend using UCSF vancomycin dosing nomogram
        i. Based on total or adjusted body weight, CrCl as in **Table 2** below
        ii. Consider deviating from nomogram if appropriate based on prior doses and levels when applicable

Table 2: Vancomycin Dosing Nomogram

LHH IV Vancomycin Dosing Nomogram				
	Use total body weight (kg) unless total BW > 120% IBW, then use adjusted BW			
CrCl (mL/min)	< 60	60-80	81-100	>100
>90 (complicated & age <65)	750 mg IV q8h	1000 mg IV q8h	1250 mg IV q8h	1500 mg IV q8h
>90 (complicated & age ≥65 or uncomplicated & age <65)	1000 mg IV q12h	1250 mg IV q12h	1500 mg IV q12h	1750 mg IV q12h
50-90	750 mg IV q12h	1000 mg IV q12h	1250 mg IV q12h	1500 mg IV q12h Complicated & age <65 1000 mg IV q8h
15-49	750 mg IV q24h	1000 mg IV q24h	1250 mg IV q24h	1500 mg IV q24h
<15	10-15 mg/kg IV x1, then redose according to levels			
CRRT	10-15 mg/kg IV q24h			
HD	5-10 mg/kg (typically 500 mg) IV post-HD (after 15-25 mg/kg loading dose, as described above)			
PD	Maintenance dose based on random levels; typically re-dosed Q 5-7 days			

Recommendations assume stable CrCl.
CRRT = continuous renal replacement therapy, e.g. CVVH, CVVHD; HD = hemodialysis; PD = peritoneal dialysis
Complicated infection (e.g. goal trough requiring 15-20 mg/L)

5. Consider calculating predicted trough if unsure of initial dose calculation
    a. Use below calculator tools (section 9) or perform calculations by hand, below:
    b. Population estimate of V_d, k_e, CL_{vanc}

$CL = k_e V_d$ $\quad$ $Vd = 0.7L/kg$ $\quad$ $CL_{vanc} = 0.75*CrCL\ (L/hr)$ $\quad$ $t_{1/2} = 0.693/k_e$

$$Cpeak = \frac{Dose/t'}{Vd * K_e} * \frac{(1-e^{-kt'})}{(1-e^{-k\tau})}$$

$Ctrough = Cpeak * e^{-k(\tau-t')}$

k, k_e = elimination rate constant $\quad$ Vd = Volume of Distribution

CL_{vanc} = vancomycin clearance $\quad$ Cpeak = predicted peak concentration

Ctrough = predicted trough concentration T' = infusion time

τ = dosing interval

6. Order Vancomycin level
    a. Typically prior to 4th dose, but there are numerous exceptions
        i. Specify date and time (approximately 30 minutes prior to scheduled dose)
        ii. Recommend ordering level during day shift when more pharmacists available to review during that time

Table 3: Guidance on Timing of Vancomycin Levels

Vancomycin Frequency	Typical Level Time
Q8h or Q12h	Trough level prior to 4th or 5th dose (prefer day shift)
Q24h (non dialysis and CRRT)	Trough level prior to 3rd or 4th dose
Intermittent Dosing by Level	Random level within 24 hours of dose (often with AM labs the following day)
Post HD	Random level prior to 2nd or 3rd dose (often with AM labs; should be drawn pre-HD)
Intermittent Dosing in Peritoneal Dialysis	Random level drawn 2 to 4 days after loading dose

    b. When to draw early (e.g. prior to 2nd or 3rd dose)
        i. Severe AKI
            1. SCr > 2-fold increase from baseline
        ii. Fluctuating renal function
            1. SCr increased by ≥ 0.3 mg/dL from baseline or ≥ 2 or 3-fold increase from baseline
        iii. Other concern for toxicity
            1. Decreased urine output
            2. Increased BUN
        iv. Concomitant nephrotoxic agents; may include, but are not limited to the following:
            1. Aminoglycosides
            2. Amphotericin
            3. IV Contrast
        v. Consider asking RN to hold next vancomycin dose until level returns if high concern for supratherapeutic level

7. Order SCr
    a. Baseline (within 24 hours of vancomycin initiation)
    b. Same day as any vancomycin level (unless on renal replacement therapy)

8. Evaluate level
    a. Drawn at steady state?

i. Usually defined as a level drawn prior to the 4th or 5th dose

b. Drawn at the appropriate time?
   i. For example, a true trough is drawn ~8 hours after the prior dose when on vancomycin Q8h or ~12h after prior dose when on vancomycin Q12h, etc.

c. Level within therapeutic range?
   i. Adjust as necessary (see tables below for guidance)

Table 4: Guidance on Vancomycin Level Interpretation

For Patients not on Dialysis or Continuous Renal Replacement Therapy

Measured vancomycin trough (mg/L)	**Goal vancomycin trough (mg/L)**	**Action***
< 5	10-15 and 15-20	Change interval and increase dose
5-10	10-15 and 15-20	Change interval or increase dose
10-15	10-15 15-20	No change Increase dose or change interval
15-20	10-15 15-20	Consider changing interval or decreasing dose No change
20-25	10-15 and 15-20	Change interval or decrease dose
> 25-34	10-15 and 15-20	Change interval and/or decrease dose; consider holding vancomycin until level < 20 mg/L
≥ 35	10-15 and 15-20	Hold vancomycin, order random level and Scr within 12 to 24 hours. Change interval and decrease dose. Resume vancomycin when level < 20 mg/L

*Assumes level is drawn at steady-state and at appropriate time relative to prior dose. Interpret other levels with caution. Typical maximum single dose is 2 grams. This is a general guidance. There may be circumstances when it would be appropriate to continue the current dose and recheck a level, particularly if the level is only slightly out of the therapeutic range.

Table 5: Guidance on Vancomycin Level Interpretation in Patients on iHD

For patients on Intermittent Hemodialysis (iHD)

Vancomycin level (mg/L) measured BEFORE HD	**Maintenance Dose to be Administered POST-HD**
< 10	1000 mg
10-15	500 – 750 mg
16-25	500 mg
> 25	Hold vancomycin x1, check level prior to next HD session and decrease post-HD dose

9. Calculate Dose Modification
   Suggested methods are listed below
   a. PK Calculator

i. Vancopk.com
ii. UCSF Adult Vancomycin Dosing (excel)

b. Linear proportion
   i. Most appropriate when modifying dose but keeping same interval
   ii. $\frac{\text{Ctrough observed}}{\text{Ctrough desired}} = \frac{\text{Current TDD}}{\text{New TDD}}$

c. Calculate based on patient specific k (see equations on following page)
   i. Using measured trough level
   ii. Population estimate of Vd
   iii. Predicted peak level

Equations to calculate patient specific PK parameters:

$k = \frac{\ln(C_{peak}/C_{trough})}{\Delta t}$ $C_{peak\ (predicted)} = C_{trough\ (measured)} + \Delta C$ $\Delta C = \frac{Dose}{V_d}$

   iv. Calculate half-life: $t_{1/2} = 0.693/k$
   v. Determine appropriate interval taking into account patient age, calculated half-life

Estimated Half-life (hours)	**Dosing Interval**
< 6	Q6h
≥ 6 and ≤ 10	Q8h
> 10 and ≤ 18	Q12h
> 18 and ≤ 24	Q24h
> 24	Consider dosing by level

   vi. Note: most adult patients will accumulate to supratherapeutic levels when using Q6h dosing intervals; exceptions may include very young, pregnant, or critically ill patients. Most elderly patients will accumulate to supratherapeutic levels when using Q8h dosing intervals; proceed with caution. Repeat predicted trough calculation if uncertain of modified dose recommendation.

10. Repeat Vancomycin trough level
   I. Every 2-3 days in patients with unstable renal function or on concomitant nephrotoxic drugs or if initial trough is at the higher end of the range.
   II. Every 5-7 days in patients with stable renal function and therapeutic levels at steady state on a stable dose
      a. More frequently as needed if signs of fluctuating renal function, such as a SCr that has consistently trended up on consecutive days or has increased or decreased by > 0.3 mg/dL in 24 hours.

Reviewed: 12/2023
Approved: X/2024