RANCHO LOS AMIGOS
NATIONAL REHABILITATION CENTER

POLICY AND PROCEDURE MANUAL
PHARMACY SERVICES

CODE: 6.07.0
DATE: 3/10/95
REVISED: 6/28/18, 4/19/22
APPROVED: Thinh Tran, Pharm. D
MEC APPROVED:11/18/09
PAGES: 1 of 6

SECTION : **CLINICAL PHARMACY SERVICES**

SUBJECT: **VANCOMYCIN MONITORING PROTOCOL**

Purpose:

1. To provide a method of dosing vancomycin that will optimize patient therapy, minimize toxicities, contain costs, and allow consistent and reliable follow through on patients' vancomycin therapy.

2. To provide an educational tool for pharmacy and medical students and residents about vancomycin monitoring and pharmacokinetics.

Background:

Vancomycin is a tricyclic glycopeptide antibiotic with activity primarily against gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA). When vancomycin was released in the late 1950s, its nickname was "Mississippi mud" because of its brownish color from impurities. Many authors suggest that the impurities may have increased the incidence of toxicities associated with vancomycin. With more sophisticated purification systems, the problem of impurities was resolved.

Since its discovery, vancomycin has had a limited role secondary to early reports of dose-related nephrotoxicity and ototoxicity and the discovery (or development) of anti-staphylococcal penicillins and cephalosporins in the mid-1960s. Vancomycin's use grew in the early 1980s with the increased prevalence of MRSA.

As regards nephrotoxicity, many recent reports in the literature have either failed to show or have found infrequent (probably < 5%) and reversible nephrotoxicity with vancomycin alone. However, investigators have found that when vancomycin is used in combination with an amino glycoside, the risk of nephrotoxicity is additive when compared with either drug alone.

Likewise, literature reports of ototoxicity associated with the use of vancomycin alone have not been well established but may occur more frequently when used in combination with the aminoglycosides or other ototoxic drugs.

Nevertheless, because vancomycin is still considered potentially nephrotoxic and ototoxic, therapeutic drug monitoring (TDM) is needed, especially in patients receiving other agents with nephrotoxic and ototoxic potential.

Approved By:

Procedure:

1. The physician may request Clinical Pharmacist assistance in the management of vancomycin therapy by placing a request for "Consult to Pharmacy" through the EHR (electronic health record) system and sending a consultation request to the Department of Medicine. Vancomycin therapy must be initiated by the requesting physician.

2. The clinical pharmacist will see the patient as soon as possible after the consultation request is received, review the patient's chart, and document the assessment and plan in the patient's EHR. The requesting physician is responsible for the vancomycin management until the patient has been seen by the clinical pharmacist.

3. If not available within the patient's EHR , the following will be ordered initially and as needed to evaluate the patient's therapy:
   (a.) Serum creatinine and BUN
   (b.) Vancomycin levels

4. To effectively inhibit sensitive infecting organisms and also avoid toxicities, the pharmacist will formulate a regimen to maintain 30 minute pre-infusion trough concentrations between 5 - 20 mg/L. Alternate levels may be used based on factors such as site of infection, the reported MIC of the infecting organism, clinical judgment, etc.

5. Drawing of Vancomycin Serum Levels:
   In order for the clinical pharmacist to make accurate calculations and adjustments, the exact time the levels are drawn must be noted. Since the bactericidal effect of vancomycin is dependent upon maintaining the serum concentration above the MIC of the infecting organism (and the MIC for susceptible organisms usually is $\leq$ 5 mcg/ml), monitoring trough levels alone is all that is necessary to assess efficacy in addition to the potential for toxicity in most patients.

Vancomycin serum levels are indicated in the following high-risk patients:

a. patients receiving other ototoxic and/or nephrotoxic drugs (e.g., aminoglycosides, amphotericin B. erythromycin, furosemide).
b. patients who remain febrile, retain an elevated WBC, and/or show signs of continued or worsening infection.
c. patients with severe renal impairment or changing renal function.
d. clinically stable patients who have been on therapy from 7 to 10 days (vancomycin trough levels will be drawn every 7 to 10 days to make sure the patients are not accumulating the drug).
e. patients in whom unusually high MIC values have been documented (MRSA, Enterococcus).

6. The Clinical Pharmacist will evaluate the vancomycin levels and adjust vancomycin dose accordingly. Dosage adjustment will follow pharmacokinetic calculations (see attachment) or base on the clinical pharmacist's clinical judgement.

7. The Clinical Pharmacist may sign-off the consultation to the requesting physician once maintenance dose for vancomycin is established. The physician may request another Clinical Pharmacist consult when necessary.

Loading Dose (LD):

LD = 25 – 30 mg/kg X Actual Body Weight

Calculation of Initial Pharmacokinetic Parameters:

1. **Definition of Weights**

TBW = total body weight
TDBW = total dry body weight or admission weight (TBW - any excess fluid)

IBW (male) = 50 kg + 2.3 [Ht (in) > 60]
IBW (female) = 45.5 kg + 2.3 [Ht (in) > 60]
Excess Fat = (TDBW -IBW)
Excess Fluid = (TBW - TDBW)

2. **Estimation of Creatinine Clearance (CrCI)**

$$\text{Clcr (ml/min/kg)} = \frac{(140 - \text{Age})}{72 \times \text{Scr}} (\times 0.85 \text{ if female})$$

3. **Estimation of Vancomycin Clearance (CI)**

Cl (L/hr) = CrC1(ml/min/kg) (0.65) (TBW) (0.06)

4. **Estimation of Volume of Distribution**

(Vd)=0.7 L/kg (TBW)

5. **Estimation of Elimination Rate Constant (Kel)** and Half-**life (T 1/2)**

$$\text{Kel (1/hr)} = \frac{C1}{Vd} \qquad T1/2 = \frac{0.693}{Kel} \text{ or } \frac{0.693\ (Vd)}{Cl}$$

6. **Choose a dosing model:** Since the majority of patients have long vancomycin half lives (> 6 hrs.) most calculations will require the BOLUS MODEL.

7. **Select appropriate τ [dosing interval] (usually between 1-2 T 1/2s) (Q12H, Q24H)**

8. **Select target trough concentration (approximately 9 + 3 mg/L)**

9. **Calculation of dose. Round dose to appropriate/realistic amount.**

$$\text{Dose} = \frac{(Cpssmin)\ (Vd)\ (1 - e^{-k\tau})}{e^{-kt}}.$$

Cpssmin = minimum steady-state plasma concentration
t = time from beginning of infusion to time of sampling (t = 11.5 hrs. when trough level is drawn 9.5 hrs after end of 2 hr infusion or 0.5 hrs before next dose and dosing interval is Q12H)

Revisions of Vancomycin Parameters after Steady State Levels are Drawn:

A. **Revision based on steady state trough only:**

1. Set Vd=0.7L/kg(TBW)
2. Revise Kel and T 1/2:

$$Kel = \frac{\ln \frac{Cpss\ tr + S(xFxD)}{Vd}}{\tau} \qquad T\ 1/2 = \frac{0.693}{Kel}$$

Cpss tr = steady-state trough plasma concentration

3. Revise Clearance (Cl);

C1= Kel (Vd)

4. Select τ [dosing interval]: (usually around 1-2 x T 1/2s) (Q12H, Q24H)

4

5. Select target trough concentration (approximately 5 -20 mg/L)
6. Calculate a new dose (round to appropriate amount)

$$Dose = \frac{(Cpss\ min)\ (Vd)\ (1 - e^{-k\tau})}{e^{-k\tau}}$$

Cpss tr = steady-state trough plasma concentration

7. Δ t = difference in time between Cpss pk and Cpss tr (in hrs).

References

1. Rybak MJ, et. al. Vancomycin Therapeutic Guidelines: A Summary Consensus Recommendations from the Infectious Diseases Society of America, The American Society of Health-System Pharmacists, the Society of Infectious Diseases Pharmacists. CID: 2009(49):325-327

2. Ambrose PE, Winter ME. Vancomycin. In Winter ME ed. *Basic Clinical Pharmacokinetics*. 4th ed. Baltimore, MD: Lippincott, Williams & Wilkins; 2004:251-27