Vancomycin Adult Model Selection Guide: Non-Hemodialysis Patients

There are currently **three vancomycin models** that can be used for dosing vancomycin in adult patients who are not receiving hemodialysis. We have prepared this guide to assist you and your staff in guideline/protocol development and DoseMeRx implementation.

Adult Non-Hemodialysis Models at a glance

	Standard Adult (1-Compartment) Buelga et al. (2005) [1]	Complex and/or Critically Ill (2-Compartment) Goti et al. (2018) [2]	Enhanced Obese (1-Compartment) Sabourenkov et al. (2019) [3]
Background	This model was developed based on a retrospective study of 215 patients receiving vancomycin treatment for a range of indications. It is a model that has been used in over 50,000 patients and has been clinically validated in several publications.	This model was derived from a retrospective study with a diverse cohort of 1,476 patients. It is particularly useful for AUC-based dosing as it fits a more complex pharmacokinetic curve that models the distribution and elimination phases of vancomycin.	This is a one-compartment, zero-order model developed and validated using 2,993 courses of vancomycin administered to patients with a body mass index (BMI) greater than 30 kg/m2. It demonstrated high predictive ability and negligible bias across all three obesity categories.
Validated Patient Parameters	Age: 18 - 100 years Height: 150 - 220 cm Weight: 40 - 200 kg	Age: 18 - 100 years Height: 150 - 220 cm Weight: 40 - 200 kg	Age: 18 - 100 years Height: 150 - 220 cm Weight: 67 - 340 kg
Utilization Percentage (Courses) [a]	75%	15%	10%
Model Switch Applicability	Complex & Critically Ill Enhanced Obese	Standard Adult Enhanced Obese	Standard Adult Complex & Critically Ill

[a] *DoseMeRx data on file*

Background: Population vs. Individualized Pharmacokinetic Models

Within DoseMeRx, there are two types of model-based dosing recommendations – a **Population-Model Based Dose** and the **Default Individualized Target** dose (i.e., the **Bayesian individualized dose)**. Both dosing recommendations are informed by the pharmacokinetic model that you have selected.

The **Population-Model Based Dose**, is the recommendation that is displayed in the absence of a vancomycin level. In this case, the dosing regimen that is recommended is adjusted based on the patient's demographics (e.g., height, weight, sex, and age) and renal function, but assumes that your patient's pharmacokinetics are similar to the population model.

However, once a vancomycin level is obtained, the model is "fitted" using Bayesian science to produce an individualized dose recommendation. In DoseMeRx, this is referred to as the **Default Individualized Target (Individualized Dose)**. This new individual model is then used to provide a patient-specific dosing recommendation to reach the desired therapeutic target.

Model Selection

Standard Adult (1-Compartment) Model

Background: Although vancomycin is typically characterized as a two or even a three-compartment model, there are numerous pharmacokinetic (PK) studies that describe a one-compartment model that are commonly used in Bayesian dosing.

A one-compartment model assumes that once a drug is administered to the patient, the drug distributes rapidly and predictably throughout the patient's body. The pharmacokinetics of the medication can then be described as if the body has one central compartment. A one-compartment model also assumes that once administration starts, elimination also starts immediately. If plotted on a graph, the elimination phase of the drug would resemble a straight line without accounting for a distribution phase.[4]

Ideal for:	• Patients with stable renal function • When a limited number of vancomycin levels are available or all or most of levels are troughs • Clinically stable patients – e.g., no significant or extreme changes in Volume of Distribution (Vd) or Clearance (Cl) observed or expected due to underlying conditions or clinical status • Adult patients between 40-200 kg (consider obese model for patients greater than 200kg)
Advantages:	• Easier to individualize since there are less parameters to fit • This the most used model within DoseMeRx
Caveats to consider:	• Makes general assumptions when calculating AUC by creating a "smoothed average" of the two compartments. • In patients with stable renal function, this is usually not clinically significant. [5]

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The standard adult one-compartment vancomycin model is widely applicable across a variety of patients. In patients that are more medically complex and/or may have underlying medical conditions that may significantly impact Vd or Cl (or both), consider one of the other models or obtain more vancomycin levels at different times during the dosing interval.

Complex and/or Critically Ill (2-Compartment) Model

Ideal for:	• Patients who are medically complex and/or clinically unstable (e.g., have significant variability in clearance or volume of distribution throughout course) • More frequent monitoring is available (i.e., more vancomycin levels can be drawn)
Advantages:	• More accurate representation of vancomycin pharmacokinetics • Better AUC estimation in patients with changing PK or who may be outside of the "average" patient
Caveats to consider:	• This model does not generally work as well with single levels or when levels are troughs

Background: Two-compartment models account for drug distribution from the central compartment to peripheral compartments. When visualizing the pharmacokinetics of a drug in a two-compartment model (on a logarithmic scale), the line is not completely linear but rather is biphasic - the first part of the line represents the drug distribution phase and the second part of the line (typically where the slope of the line

changes) represents the elimination phase. Accounting for this period of drug distribution allows for greater accuracy in the area-under-the-curve (AUC) prediction in patients who are critically ill with rapid shifts in fluid status and renal function.[4]

To improve the predictive reliability of a two-compartment model, two drug levels obtained at different points are recommended, at least initially. These points can either be during the same interval or can be two levels obtained at different times during different intervals. After this initial fit, ongoing therapy can be periodically assessed using single levels.

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The ideal clinical scenario for this model is in patients that will be monitored more frequently such as unstable patients or when it necessary to account for medical conditions which may result in unusual vancomycin pharmacokinetics (e.g., amputees, fluid loaded, septic patients, patients on vasopressors).

Enhanced Obese (1-Compartment) Model

Background: The enhanced obese vancomycin model is a one-compartment, zero-order absorption model developed and validated by DoseMeRx using 2,993 courses of vancomycin administered to patients with a body mass index (BMI) ≥30 kg/m2. The enhanced obese model utilizes the patient's ideal body weight (IBW) for creatinine clearance and volume of distribution calculations.[3] It demonstrated a higher predictive ability when compared to the standard obese model.

Ideal for:	• Patients with higher BMIs (and weights up to 340kg) • Patients with stable renal function • When limited vancomycin levels are available
Advantages:	• More accurate vancomycin dosing in obese patients when compared to other models since it was specifically designed for use in patients who are obese
Caveats to consider:	• Makes some general assumptions when calculating AUC by creating a "smoothed average" of the two compartments. In patients with stable renal function, this is usually not clinically significant. [5]

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This model is ideal for patients with a BMI of 30 kg/m2 and above but performs especially well with higher BMIs (e.g., 40kg/m2). It is also the model of choice for patients who weigh between 200 and 340kg.

In patients with changing renal function or clinical instability, consider obtaining multiple levels at different times periodically throughout the course. These levels do not have to be at a specific time or within the same dosing interval.

Model Fit and Interchanging Between Models

There are always patients that may be outliers and clinical decisions may guide a user to look at more than one model for a patient. In some cases, one model may "fit" better than another. This can be easily visualized using the Historical Plot graph. However, if you suspect that the first model that you have selected does not fit the patient well, then we suggest the following:

Tips for improving model fit

1. **Double check** that lab results, patient demographics, and dosing information are correct.
2. **Consider obtaining another level** at a different time point (relative to dose administration).
3. If there is evidence that the patient's pharmacokinetics have shifted substantially (e.g. significant change in clearance and/or volume of distribution) **consider deselecting older drug levels** that may no longer be representative of the patient's current clinical status.
4. **Consider switching** to a different model.

Note: Model fit should always be reviewed in combination with the Historical Plot, regardless of the results displayed in the indicator. This information is not intended to supersede clinical judgment.

Helpful FAQs

For more information about model selection, check out the DoseMeRx Help Section.

References

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