



How to Communicate the Changes to Your Prescribers

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Take the Opportunity to Steward Vancomycin with Release of 2020 Vancomycin Dosing Guidelines



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The [2020 vancomycin monitoring guidelines](#) were released in March during the COVID-19 pandemic response and therefore under the radar of many physicians.

They recommend a shift away from [vancomycin trough levels](#) to Area Under the Curve (AUC), in relation to the minimum inhibitory concentration (MIC) in adults, pediatrics, and neonates.

This dosing approach is recommended for patients with serious infections due to Methicillin-resistant *Staphylococcus aureus* (MRSA).

There are a number of studies demonstrating the clinical impact associated with inappropriate vancomycin dosing in many patients with MRSA infections utilizing trough levels alone, particularly ICU patients with renal insufficiency and obesity.

When vancomycin levels are suboptimal, treatment failures can occur due to isolates that have intermediate susceptibility to vancomycin or isolates that are resistant to vancomycin.

When dosing is too high, patients risk vancomycin-induced nephrotoxicity, which ranges from 5 to 43% with a relative risk of 2.45 (95% Confidence Interval: 1.69-3.55) based on clinical studies.

Vancomycin dosing based on AUC:MIC is now recommended as the optimal dosing and monitoring method for the treatment of serious MRSA infections.

Dosing by AUC:MIC (as determined by broth microdilution) with a goal of 400-600 mg-hr/L should keep vancomycin concentration at therapeutic levels needed to achieve a clinical response, but below levels that might increase the risk of nephrotoxicity.

Methods of Calculating AUC:MIC

Bayesian Dosing Approach

Methods of calculating AUC include an equation-based methodology or a [Bayesian approach](#), which utilizes population data to calculate a patient's pharmacokinetics.

The Bayesian method, available through commercially available software programs, allows for precision dosing by creating an individualized, dynamic model of dosing vancomycin for every patient that can be updated over time as more patient specific information (e.g. vancomycin levels, serum creatinine) is received.

According to the [2020 vancomycin dosing guidelines](#), the preferred approach to monitoring AUC is through these programs. This recommendation was given an A-III GRADE. Bayesian software programs (such as DoseMeRx) can utilize drug levels obtained earlier in therapy (e.g. 24-48 hours) because it is not required that a patient's vancomycin levels be stable, otherwise known as "steady state". One recent [study](#) documented the transition from conventional trough-based vancomycin dosing to dosing AUC based dosing (targeting an AUC of at least 400) at four adult hospitals. A Bayesian analysis of a subgroup of AUC and trough guided patients in this study indicated that vancomycin exposure was significantly higher in the trough guided dosing group. The authors concluded that AUC-guided dosing resulted in lower daily vancomycin doses and lower trough and AUC values. From a safety standpoint, AUC-guided dosing of vancomycin was associated with reduced nephrotoxicity, which appeared to be a result of reduced vancomycin exposure.

First Order Kinetic Calculations

Another method that can be utilized to calculate AUC is by using first order kinetic calculations. Practically speaking, to make patient-specific adjustments to the vancomycin dose, two vancomycin levels within the same dosing interval are needed.

Unlike Bayesian dosing, this methodology requires patients to be at steady state when the levels are drawn.

The first level is obtained 1-2 hours after the end of the infusion (the peak) and the second level should be obtained prior to the next dose. With this information, a calculation can be made to adjust subsequent doses of vancomycin. [Monitoring](#) is recommended for patients with serious MRSA infections, but also all patients at high risk for nephrotoxicity (e.g., critically ill patients receiving concurrent nephrotoxic therapy), patients with unstable renal function, and those receiving prolonged courses of therapy (> 3 to 5 days).

Frequency of monitoring is based on clinical judgment but general recommendations are outlined:

- Early monitoring when doses exceed 2-3 grams per day in pediatric patients
- Close monitoring in pediatric patients with poor or augmented renal function
- Daily monitoring in hemodynamically unstable adults
- Weekly monitoring in hemodynamically stable adults



How can you prepare physicians for the conversion to AUC for vancomycin?

Educate Your Physicians

- It is important that all clinicians in your institution understand **why and when this switch in dosing strategy** will take place and to ensure that your pharmacists have been trained on this pharmacokinetic dosing strategy.
- Clinicians must expect **vancomycin levels to be drawn more frequently in the first 24-48 hours** of hospitalization to adjust the second dose of treatment.
- It will be especially important for **Emergency Department clinicians, intensivists and hospitalists** to understand this transition is happening, so they can facilitate vancomycin draws in the first 24-48 hours of hospitalization.
- Clinicians should not be concerned when vancomycin levels **are lower than what is typically observed with trough based dosing**. It is not uncommon to see patients with a lower trough level who are still in the therapeutic AUC:MIC range.



- If not already in place at your institution, **all clinicians should be in touch with pharmacists** regarding all patients receiving vancomycin. Consider having discussions with your pharmacy team if the volume status or clearance of a patient changes significantly, perhaps requiring a recalculation of their vancomycin dosing.

Involve the Entire Care Team

- **Nurses:** Not only do physicians and other prescribers need to be educated about this new dosing strategy, but nurses must also be made aware so they understand they are no longer drawing trough levels but rather providing therapeutic drug monitoring that is less reliant on timing and frequency.
- **Laboratory Staff:** It is important to make laboratory staff and phlebotomists aware of these changes as it will change the practice of obtaining levels. For first order kinetics, there will be a need for more labs since two levels will have to be drawn for each AUC calculation. It is important that anyone drawing the vancomycin level document the exact time the level is being drawn as well as the dose of vancomycin at the time, in order for the AUC:MIC to be calculated accurately. For hospitals utilizing Bayesian dosing, the practice will be different since in many cases they can obtain a single level and the level can be obtained at any point in the dosing interval so the accuracy of timing is less relevant. Preparing hospital staff in advance of these changes will prevent confusion when an inpatient requires vancomycin.

Review Patient Discharge Policies

- In order to ensure discharge and transitions of care are smooth for patients on vancomycin, it is important to find out how accepting facilities in your region such as subacute skilled nursing facilities, long-term acute care hospitals, and infusion centers are managing the guideline change.
- If there is advanced communication and preparation, it will save time at discharge and help facilitate discharge to one of these facilities or centers.
- The patient may be stable at discharge such that additional AUC:MIC do not have to be calculated.
- It is important to enable the discharge team to spend adequate time outlining discharge dosing for vancomycin in order to ensure successful discharge. If patients are transitioning to home health, it is probably not reasonable to expect that home health agencies will be able to dose to AUC; the hospital pharmacy may give instructions to home health on monitoring weekly levels and dosing accordingly.

Hospital antibiotic stewardship programs should take this opportunity to focus on strategies to improve the use of this important Gram-positive agent and not reflexively place all critically ill patients on vancomycin for methicillin-resistant *Staphylococcus aureus* treatment.

Antibiotic Stewardship Committees should dedicate time to educating themselves on this change and how it applies to their own institution, but then also develop a dedicated education strategy targeting hospital clinicians.

Antibiotic stewards can assist the change management process by helping to educate prescribers on the new dosing protocols.

Stewards can also emphasize the opportunity to improve the hospital's utilization of vancomycin.



Summary

These are some activities physicians and pharmacists can engage in now to prepare for the vancomycin dosing change:

- ✓ **Educate clinicians** focusing on Emergency Department physicians, intensivists, hospitalists and house staff on this change in practice
- ✓ **Discuss with pharmacy** what their strategy will be once the new dosing guidelines are released and whether clinical pharmacists have been adequately serviced on how to calculate the AUC:MIC
- ✓ **Educate hospital staff** including nurses and laboratory personnel emphasizing the draws in the first 24-48 hours of hospitalization and when there is a significant change in renal function or volumic status of the patient
- ✓ **Discuss with regional accepting facilities and infusion centers** how they are handling the change in guideline and agree on an approach to facilitate smooth transitions
- ✓ **Ensure the hospital antibiotic stewardship program** highlights vancomycin stewardship during this transition



It is critical to work with your teams closely to determine who can assist or carry out any of the tasks above, based on their comfort level with interacting with clinicians and regional facilities.

In antibiotic stewardship, we are rarely given an opportunity to improve use of an antibiotic across all US hospitals at once. Let's take this opportunity to steward one of our most valuable therapeutic options – when hospitals will be re-evaluating their dosing strategy for vancomycin.



“It’s a straight-forward way to implement AUC-based decision making in vancomycin dosing whilst at the same time minimizing the number of levels needed. It’s a win, win... DoseMeRx solves my need.”

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