Clinical experience and guidance for organizational implementation of VANCO READY™ vancomycin injection premix solution

Review of efficiencies and patient care with a ready to use, room temperature stable vancomycin injection

About the Author

Cody Parsons PharmD, BCCCP, APh is the Manager of Clinical Operations for the Cardiovascular Health Destination Service Line at a tertiary academic medical center in northern California. As the Department of Pharmacy clinical expert focused on patient-first care, Cody utilizes cost-effective and evidence-based approaches to effectively operationalize medicine through EPIC electronic medical record systems for a large research-based hospital setting of over 600 patient beds.

Background

The pharmacy is increasingly evaluating and adopting new products and processes to ensure adherence to patient-first care initiatives including enhanced patient outcomes and safety. New products that reduce time to administration and free up pharmacists and technicians to perform other tasks within the pharmacy are thoroughly evaluated and considered for organizational implementation.

The Objective

We evaluated Xellia's vancomycin injection premix solution, VANCO READY, for its ability to mitigate supply chain inefficiencies and reduce incremental hospital waste. Previous delivery mechanisms including frozen, batched compounding, and on-demand compounding require additional steps to administration and complicate pharmacy operations. For patients in the clinical setting with serious life-threatening infections, a room-temperature stable solution that can be stored in automated dispensing cabinets helps improve time to first dose and aligns with cost-effective and evidence-based care principles.

VANCO READY does carry a boxed warning for embryo-fetal toxicity due to the excipients used to stabalize the solution in room-temperature conditions. Due to this unique safety consideration, we also needed to evaluate our ability to safely implement this formulation of vancomycin injection.

The Challenge

Previous vancomycin injection delivery mechanisms contribute to 2 major areas of concern:

1. Supply concerns

Sourced from outside suppliers, product is susceptible to unpredictable supply challenges:

- Last-minute supply shortages
- Changes in suppliers
- Inconsistencies in dose format for each dose

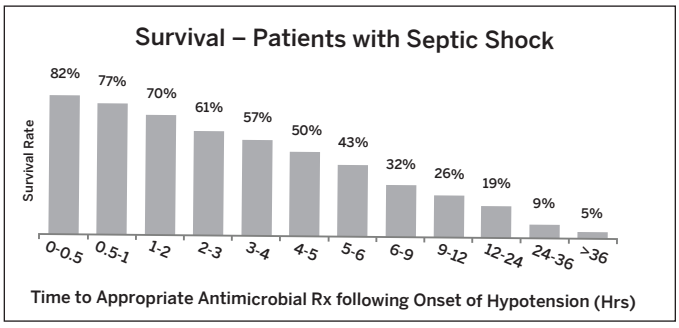
2. Workflow concerns

Pharmacy staff must take additional actions to project, thaw, compound, label, store, and deliver product to the floors, which leads to significant workflow disruptions:

- Increased workload on central IV rooms
- Limited freezer and refrigerator storage
- Batching additional product based on historical data

Clinical Significance

Supply chain inefficiencies and workflow disruptions jeopardize our patient-first service-level commitment of 15-minute vancomycin delivery to nurses. It is important that we consistently meet this service-level commitment so that our hospital can stay compliant with guidelines set by the Centers for Medicare and Medicaid Services (CMS) and the Surviving Sepsis Campaign. These guidelines are clinically important to our patients because it has been shown that each hour delay in antibiotic administration for patients in septic shock increase mortality by a mean of 7.6%.



Reference: Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med.* 2006;34(6):1589-96.

Additionally, these inefficiencies contribute to additional hospital waste and staff expenditures.

VANCO READY™ Investigation Process

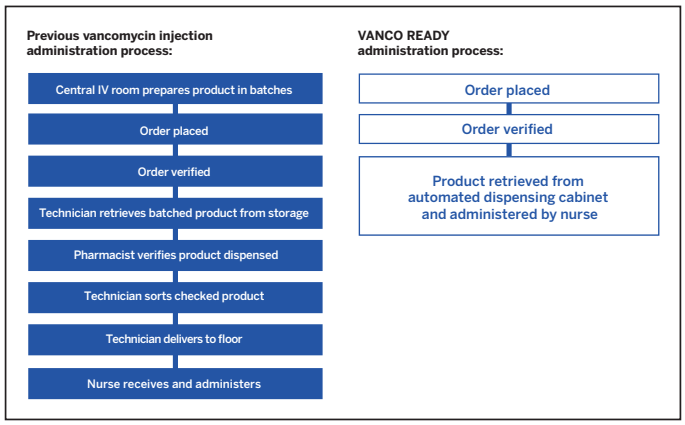
To begin evaluating VANCO READY for organizational implementation, we consulted primary stakeholders across the organization. Anyone who stands to be directly affected, either positively or negatively, by the outcomes of VANCO READY implementation is considered a primary stakeholder:

- Pharmacy leadership
- Clinical pharmacists
- Supply chain pharmacy managers
- Pharmacy purchasing
- Medication Safety
- EPIC application analyst
- Operating room, infectious disease, and emergency room departments

Throughout the consultative investigation process we focused on 3 key areas of clinical improvement; patient needs, pharmacy staff workflows, and product performance.

Patient Needs Evaluation

To align with patient-first care initiatives, VANCO READY was evaluated on its ability to improve early intervention from time of medication order to administration for critically ill patients. The goal is to guarantee strict adherence to a 15-minute service level commitment for vancomycin injection delivery to front-line staff.



Pharmacy Staff Evaluation

Reducing supply chain inefficiencies was our number one priority to free up pharmacists and technicians for other tasks within the pharmacy. VANCO READY was evaluated for its impact on staff workflows.

- **No labor for central IV rooms**
- **No product to batch**
- **No product to store in freezers or refrigerators**
- **No additional hospital waste**

Product Performance Evaluation

VANCO READY is supplied as a shelf-stable, ready to use vancomycin injection, which reduces the risk of contamination and compounding errors. But operationalizing the boxed warning regarding risk of embryo-fetal toxicity in pregnant individuals presented 3 points of concern, weighed as risk vs. benefit:

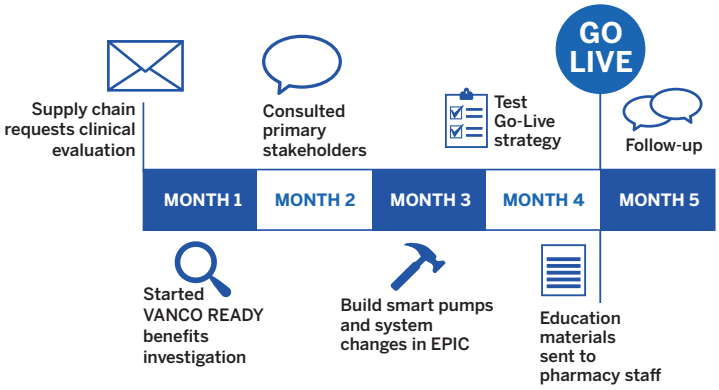
1. *Can we get it to the patient safely?*
2. *What is the process for catching urgent cases on the front-line?*
3. *How do we ensure all stakeholders are on the same page?*

Decision to utilize VANCO READY:

It was identified that women of child-bearing age accounted for a small percentage of the vancomycin patient population and that implementing a dispense logic build in the EPIC could ensure safe product delivery to all patients in the clinical setting.

VANCO READY™ Implementation

Because VANCO READY cannot be administered to pregnant women, a comprehensive implementation strategy is required to ensure proper dosing. To streamline the process, we identified one point-of-contact for the pharmacy department who worked closely with one point-of-contact for the EPIC team. The entire process from first contact to go-live took less than 4 months.



System Updates

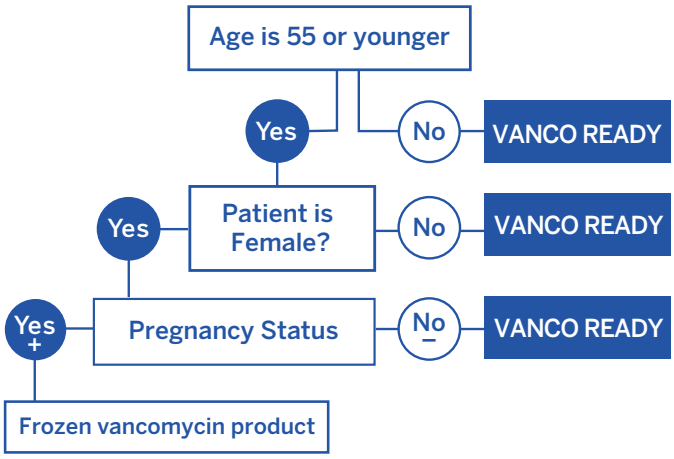
Working closely with the EPIC point-of-contact we created our builds for both the EPIC electronic medical records system and the smart I.V. pumps. Our primary objective was to ensure safe medication delivery by narrowing the chances of programming errors and instituting a safe use system that uses heavy dispense logic as an additional safety barrier to medication alerts.

Epic System Build with Automated Dispense Logic

The EPIC build considered the process by which vancomycin is ordered and administered. VANCO READY is stocked in automated dispensing cabinets to reduce the time to first dose for severe life-threatening infections but all patient information and lab results are not always known at the time of vancomycin administration. The EPIC system needed to seamlessly handle these cases. We explored multiple strategies to ensure safe use of VANCO READY, including: alerts that would warn of use in pregnancy during order entry and verification, adding discrete fields in the vancomycin order or consult where the provider would be required to capture pregnancy status, and utilizing available dispense logic functionality. In the end, we decided the best way forward would be to utilize EPIC dispense logic to evaluate patient demographic information to aid in vancomycin product selection at the time of order verification.

A purposeful safety barrier was implemented that allowed the physician to order intravenous vancomycin (i.e. "orderable"), but not choose the specific vancomycin product (i.e. "dispensable"). When the order is received by the pharmacy, the system defaults to VANCO READY and utilizes dispense logic to drastically reduce the amount of alerts and disruptions to the pharmacy staff:

VANCO READY EPIC Dispense Logic



Through VANCO READY dispense logic pharmacists are not responsible for manually determining which vancomycin product to dispense for the patient. The EPIC build allows the system to review patient pregnancy status and switch to a more appropriate delivery mechanism if pregnancy status is positive or unknown, significantly decreasing the pharmacists' workload.

Medication alerts from our third party alert vendor are still activated for VANCO READY as a safety net to the dispense logic build. However, the dispense logic is accurate and these alerts are only seen when the pharmacist chooses to utilize VANCO READY in a patient without a pregnancy status documented in EPIC, but it is determined that the patient is truly not pregnant and can receive the product safely.

Smart I.V. Pump Build

The built-in drug library and the dose error reduction system provides the necessary safety protocols to mitigate human error. In adding VANCO READY to the smart pump, new concentrations were programmed and their corresponding barcodes added to the software system.

Automated Dispensing Cabinets

Technicians created space and stocked VANCO READY in the automated dispensing cabinets. To ensure VANCO READY could not be taken from an automated dispensing cabinet and administered to a pregnant patient, we ensured the following: VANCO READY would not be available on override and VANCO READY would not be stored in an automated dispensing cabinet on inventory mode. These two rules would ensure that each VANCO READY dose would be pulled from the automated dispensing cabinet against a profiled and verified medication order for each patient.

Barcode Medication Administration

As a final safety barrier, we ensured that VANCO READY would not barcode scan on an order for an alternative vancomycin product upon medication administration at the bedside. This same logic was also applied to IV dispensing software and automated dispensing cabinet software.

Unique Area of Use

The system builds described above provide the safety protocols necessary to ensure patient-first care objectives are met. However, in the operating room orders are not subject to dispense logic and therefore a different strategy was instituted to ensure safe medication delivery. The operating room strategy relies on front-line staff to perform the necessary safety precautions for VANCO READY.

- Antimicrobial prophylaxis screening scripts in the OR satellite pharmacy were updated to include a question regarding pregnancy status
- Nurse flow sheet is reviewed to determine pregnancy status
- If the patient is not pregnant pharmacists will distribute VANCO READY from the OR satellite pharmacy
- VANCO READY was not stocked in automated dispensing cabinets, which were set to inventory mode

Go-Live

Once all systems were built and VANCO READY was ready to be operationalized we followed a simple 5 step process for roll-out across the organization.

Step 1: Complete testing in the environment

Step 2: Medication Safety sign off

Step 3: Technicians create space and stock product in automated dispensing cabinets

Step 4: SBAR education to pharmacy staff

Step 5: Go-Live!

Room-temp Vancomycin Premix

(Go-Live 09/2019)

Situation:
The organization is bringing on a new preparation of premixed intravenous vancomycin (in sterile water) that is stable at room temperature. Initially, we will carry the 1g and 1.5g sizes with 2g to follow in late September. The new preparation comes with the following FDA boxed warning:

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF EMBRYO-FETAL TOXICITY DUE TO EXCIPIENTS

This formulation of Vancomycin Injection is not recommended for use during pregnancy because it contains the excipients polyethylene glycol (PEG 400) and N-acetyl D-alanine (NADA), which caused fetal malformations in animal reproduction studies. If use of vancomycin is needed during pregnancy, use other available formulations of vancomycin. (5.1, 8.1)

Background:
The organization compounds multiple preparations of intravenous vancomycin in addition to purchasing refrigerated premix vancomycin at a premium. Notably, the compounded preparations require refrigeration as well. The compounded intravenous vancomycin poses several inefficiencies- please see below:

1. **Increased time for the antibiotic to reach the patient. This is secondary to the need for refrigeration and limited dispensing cabinet refrigerator space.**
2. **Increased waste secondary to short life of compounded product.**
3. **Significant workload for our IV room staff.**
4. **Significant cost associated with compounding, waste, and refrigerated premix.**

Assessment:
Bringing on the new room temperature vancomycin product will decrease IV room workload, waste, and cost while making the product more accessible to nursing (storage in the dispensing cabinets). The preparation does carry a risk for expecting mothers and EPIC safeguards will be necessary to prevent dispensing of this product to that population.

Recommendation:
We will go-live with the new room temperature vancomycin in sterile water preparation in September 2019. EPIC safety measures will be present within the order and will auto select the correct product based on numerous factors including sex, age (<55), and pregnancy status.

**Note: If the pharmacist manually changes back to the vancomycin in sterile water preparation on a patient that EPIC has pregnancy status of 'unknown' but is within childbearing age a "Pregnancy Alert" will fire to assure that the change is intentional and the pharmacist has confirmed the patient is NOT pregnant.

Parsons, C 2019

Post-Implementation

VANCO READY went live across our organization in early September 2019. Since its implementation, follow-up assessments have been used to measure its impact in the clinical environment.

Safe Use Assessment

Our system for reporting medication safety errors such as a pregnant person being administered VANCO READY have confirmed there are no reports on record.

Staff Assessment

Satisfaction with VANCO READY on patient-first care as reported by staff in all departments demonstrates a positive impact on former supply chain inefficiencies and hospital waste. Staff report less labor required to compound, label, and deliver vancomycin across the hospital which helps streamline distribution and provides more time to address other tasks.

Organizational Assessment

Implementation of VANCO READY has seen a significant reduction in labor and waste costs associated with frozen and compounded product. Its impact is in-line with cost-effective care and evidence based principles.

Conclusion

VANCO READY supports patient-first care initiatives for patients with serious life-threatening infections but proper implementation into the environment is critical. The EPIC system allows for heavy dispense logic utilization which advances product selection beyond medication alerts. If done properly, implementation is simple and effective.

After operationalizing VANCO READY across the organization, results have shown reduced supply chain inefficiencies and pharmacists and technicians have been freed up for other tasks within the pharmacy. The organization has also seen a significant reduction in hospital waste from previous delivery mechanisms including frozen, batched compounding, and on-demand compounding.

VANCO READY plays an important role for institutions in support of cost-effective care and evidence-based care principles.

Important Safety Information

VANCOMYCIN INJECTION

INDICATIONS AND USAGE

Vancomycin Injection is a glycopeptide antibacterial indicated in adult and pediatric patients (1 month and older) for the treatment of:

- Septicemia (1.1)
- Infective Endocarditis (1.2)
- Skin and Skin Structure Infections (1.3)
- Bone Infections (1.4)
- Lower Respiratory Tract Infections (1.5)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancomycin Injection and other antibacterial drugs, Vancomycin Injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. (1.6)

IMPORTANT SAFETY INFORMATION

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This formulation of Vancomycin Injection is not recommended for use during pregnancy because it contains the excipients polyethylene glycol (PEG 400) and N-acetyl D-alanine (NADA), which caused fetal malformations in animal reproduction studies. If use of vancomycin is needed during pregnancy, use other available formulations of vancomycin. (5.1, 8.1)

DOSAGE AND ADMINISTRATION

Use this formulation of Vancomycin Injection only in patients who require the entire (500 mg, 1 g, 1.5 g or 2 g) dose and not any fraction thereof. (2.1)

For intravenous use only. Do Not administer orally.

Administer Vancomycin Injection by intravenous infusion over 60 minutes or greater to reduce the risk of infusion reactions (2.1)

Adult Patients: 2 g divided either as 0.5 grams (g) every 6 hours or 1 g every 12 hours (2.2)

Pediatric Patients (1 Month and Older): 10 mg/kg per dose given every 6 hours (2.3)

Patients with Renal Impairment: See full prescribing information for recommended doses in patients with renal impairment (2.4)

See full prescribing information for further important administration and preparation instructions (2.1, 2.5)

DOSAGE FORMS AND STRENGTHS

Vancomycin Injection: Single-dose flexible bags containing 500 mg vancomycin in 100 mL, 1 g vancomycin in 200 mL, 1.5 g vancomycin in 300 mL and 2 g vancomycin in 400 mL of liquid (3).

CONTRAINDICATIONS

Hypersensitivity to vancomycin (4)

WARNINGS AND PRECAUTIONS

Infusion Reactions: Hypotension, including shock and cardiac arrest, wheezing, dyspnea, urticaria, muscular and chest pain and "red man syndrome" which manifests as pruritus and erythema that involves the face, neck and upper torso may occur with rapid intravenous administration. To reduce the risk of infusion reactions, administer Vancomycin Injection over a period of 60 minutes or greater and also prior to intravenous anesthetic agents. (2.1, 5.2)

Nephrotoxicity: Systemic vancomycin exposure may result in acute kidney injury (AKI) including acute renal failure, mainly due to interstitial nephritis or less commonly acute tubular necrosis. Monitor serum vancomycin concentrations and renal function. (5.3)

Ototoxicity: Ototoxicity has occurred in patients receiving vancomycin. Monitor for signs and symptoms of ototoxicity during therapy. Monitor serum vancomycin concentrations and renal function. Assessment of auditory function may be appropriate in some instances. (5.4)

Clostridium Difficile-Associated Diarrhea: Evaluate patients if diarrhea occurs. (5.5).

Neutropenia: Periodically monitor leukocyte count. (5.7)

Phlebitis: To reduce the risk of local irritation and phlebitis administer Vancomycin Injection by a secure intravenous route of administration. (5.8)

Development of Drug-Resistant Bacteria: Prescribing Vancomycin Injection in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria. (5.9)

ADVERSE REACTIONS

The common adverse reactions are anaphylaxis, "red man syndrome", acute kidney injury, hearing loss, neutropenia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Xellia Pharmaceuticals USA, LLC at 1-833-295-6953 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Anesthetic Agents: Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing. (2.1, 7.1)

Piperacillin/Tazobactam: Increased incidence of acute kidney injury in patients receiving concomitant piperacillin/tazobactam and vancomycin as compared to vancomycin alone. Monitor kidney function in patients (7.2)