Infinium Pharmacy's Switch to VANCO READY® Vancomycin Injection, USP: Reducing Potential Errors and Increasing Benefits to Patients in Long-Term Care Settings

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Infinium Pharmacy

Infinium Pharmacy is a privately owned and independently operated, long-term care pharmacy, dedicated to personalized pharmaceutical care in skilled and assisted living facilities. The pharmacy was opened in 2017 starting with two skilled nursing facilities. Infinium Pharmacy now has two locations in both St. Louis and Springfield, Missouri and is currently servicing 8,500 beds in over 80 nursing facilities.

Vancomycin: Challenges to Compounding for Infinium Pharmacy

In skilled nursing settings, the acuity and complexity of admissions continue to rise. It is common for rehabilitation patients and residents recently discharged from hospital settings to have complex medication regimens. The capability of skilled nursing centers to manage and administer medications for complex conditions has risen as well and, often, this capability allows residents to avert hospitalizations.

At Infinium Pharmacy, as with all long-term care pharmacies, many intravenous vancomycin orders are filled each year with the number continuing to increase. The most common indications for vancomycin treatment are osteomyelitis, lower respiratory tract infections, infective endocarditis, septicemia, and skin and soft tissue infections. Vancomycin administration is dependent on the type and location of the infection. Since vancomycin has poor oral bioavailability, its administration via the intravenous route is most often used to treat various systemic infections.[1]

Intravenous vancomycin injection can be used to treat MRSA (Methicillin Resistant Staphylococcus Aureus) infections and other infections caused by susceptible gram-positive organisms. For intravenous administration, it is available as a frozen product, a sterile powder for compounding/reconstitution, as well as a room temperature premix formulation.[1]

In the past, vancomycin was restricted to skilled nursing facilities that could manage laboratory requirements and administer time sensitive compounded intravenous medications. Innovation in the dosing, production and packaging of vancomycin has made it more accessible to pharmacies and skilled nursing homes—and easier to manage. Vancomycin can now be monitored using laboratory data drawn at any time during the day, and, products have been developed that don't require complex compounding, storage, and handling requirements.

Pharmacies, regardless of setting, still function primarily on the revenue and costs model associated with the dispensing of medications. Intravenous medications are generally expensive for a multitude of reasons, in part, because providing these therapies are complicated, and often requiring complex dosing and sterile compounding. These products can also have special storage, handling, administration, and monitoring requirements. For vancomycin, each of these variables are critical to consider as part of treating an infectious disease.

In 2019 Infinium Pharmacy made the decision to use VANCO READY® Vancomycin Injection, USP for residents in their skilled nursing facilities. Their rationale to choose VANCO READY® was based on the availability of doses, the ease of storage and handling, and the return on investment.

Frozen premixed vancomycin is only available in 500 mg, 750 mg, and 1 g strengths. Because of the limited doses available, along with the pharmacy's inability to meet the temperature storage requirements, it was decided that Infinium would not carry the frozen product line.

Bag-to-vial systems can involve a more complicated activation process. Several of Infinium Pharmacy's long-term care facilities complained about inconsistent operation of these systems and requested compounded vancomycin doses instead. Infinium Pharmacy's cleanroom installation was still in progress, so all compounded vancomycin orders had to be outsourced to an infusion pharmacy. Outsourcing resulted in more expensive product and delays in therapy getting to the patient, caused by issues with product shipment.

The VANCO READY premixed vancomycin formulation offered a product that required no thawing, compounding, or activating and was available in seven doses from 500 mg to 2 g.

Switching to a room-temperature premixed solution was a clear choice for Infinium Pharmacy.

Potential Benefits and Limitations Considered

VANCO READY® Vancomycin Injection, USP has a boxed warning and is not to be used during the first and second trimester of pregnancy, due to excipients. If vancomycin is needed during pregnancy, other available formulations should be used. See last page for Important Safety Information. For full prescribing information, including boxed warning, please visit www.vancoready.com.

Labor and organization. The first consideration the pharmacy undertook was assessing the time associated with vancomycin preparation. Switching from a bag-to-vial system to a room temperature stable premixed solution meant a possible reduction in labor and time, and this was appealing to both the pharmacy and the nursing facility decision makers. They discovered that it takes less time to dispense a VANCO READY product than other vancomycin formulations. The bag-to-vial systems require vials, bags, and connectors, and take time to assemble. These also push some of the labor of activating the system onto facility nursing staff, creating a time burden and opportunities for error. Compounding vancomycin at the pharmacy requires the greatest amount of pharmacy labor time to prepare and dispense, in addition to the certifications necessary for a pharmacy to set-up a clean room and abide by the litany of regulations around their operations.

The next consideration the pharmacy made involved assessing the product's ease-of-use for pharmacy staff. Both the room temperature stable premixed product and compounded product are similar in terms of long-term care staff administration. The main difference, in addition to the effort required to compound, is that compounded vancomycin has a shorter beyond-use date and needs to be removed from refrigeration and warmed to room temperature, prior to infusion.

Due to a lack of freezer storage space for frozen premixed products, Infinium Pharmacy did not stock the frozen formulation of vancomycin. Frozen premixed products need to be kept frozen during transport to the long-term care facility and remain frozen prior to use. The frozen product then requires thawing prior to dispensing, so it can be infused. Because of these requirements, it was not feasible to carry frozen vancomycin in the long-term care facilities served by Infinium. VANCO READY® Vancomycin Injection, USP, on the other hand, being room temperature stable, is quickly available for administration.

Price. Janice Cerotti, the Director of Operations at Infinium Pharmacy, did not see a significant difference in price between how they used to provide vancomycin (bag-to-vial systems) and the VANCO READY product. Vancomycin doses are not necessarily expensive by themselves, but the entire course of therapy is expensive because it usually continues for several weeks and requires frequent lab monitoring. Vancomycin may be less expensive when compounded (depending on the dose), but that is without considering the costs of the labor and supplies to compound a sterile product properly.

Short training time. When determining the amount of time it would take to train staff on this new product, they found that the training process for VANCO READY took only a few minutes. The process was straightforward, according to Cerotti, who believes that VANCO READY is a fantastic option for last-minute orders and for high volume locations—who may consider storing the product in an emergency supply cabinet.

Longer stability. For Infinium Pharmacy, the beyond-use dating of the room temperature stable vancomycin is somewhat comparable to a bag-to-vial product, although the considerations around different components and whether they come connected or not creates some confusion and limitations. Room temperature vancomycin has a much longer shelf life than that of a compounded vancomycin product, given the sterility risk levels in the state of Missouri, which limit compounded vancomycin to seven-days. (Compounding risk levels dictate the beyond-use dating and can vary by state and by class of sterile environment where compounding takes place.)

Safety and first-dose kits. While the pharmacy does not supply vancomycin in first-dose kits at the facilities Infinium services, it could be an option for some. Since Infinium Pharmacy's company policy and their client mix do not support storing infusion pumps in emergency supply cabinets, they do not utilize premixed vancomycin as part of their emergency kits. The frequency of use by high volume rehabilitation long-term care facilities and the consistent availability of infusion pumps on site in the nursing center may change the decision with respect to storing premixed vancomycin in emergency supply cabinets.

Key Stakeholders and the Decision-Making Process

Complaints. Prior to switching to VANCO READY, Infinium Pharmacy was frequently receiving complaints about the difficulty of activating bag-to-vial systems (and wasted doses). They were also hearing negative comments regarding the time it took for the outsourced compounds to reach the facilities. To date, the pharmacy has not received any complaints about VANCO READY, which emphasizes how well the product has been accepted by pharmacy and nursing staff.

Avoiding the potential for errors. Activating bag-to-vial systems are not without the potential for failure.[2-4] Although relatively rare, the potential for mistakes can occur when improperly connecting and mixing the bag-to-vial system. Another issue that arose with bag-to-vial systems was incorrect dose administration (facility error, not pharmacy error). The potential for medication errors may exist because two bags may be needed to make the total dose (i.e., 2 x 1 g bags to equal a 2 g dose) with the initiation of the second bag inadvertently being forgotten. The bag-to-vial system may also fail if the connection isn't fully made, and the combination of the intravenous fluid and powdered medication isn't fully mixed. According to the Food & Drug Administration (FDA), there is a 1 in 10 error rate associated with compounding.[2-5] With the room temperature stable premixed formulation, there is nothing to activate and mix, and multiple bags should not be necessary to make up a total dose, as VANCO READY is available in the seven most common adult doses.

Elimination of wasted doses and delays in therapy. When using other vancomycin products, the drug can be wasted by improper docking of the vial, connector, and diluent bag. One of the main concerns of pharmacists and nurses is that wasted doses can cause delays in therapy. Also, the room temperature premixed solution allows the clinical staff to make quick dose adjustments without wasting product, while minimizing delays in the start of therapy.

Boxed warning. VANCO READY carries a boxed warning regarding the risk of fetal toxicity during use in the first and second trimesters of pregnancy. This warning does not apply to the majority of the long-term care patient population as most residents are beyond their reproductive years. For that reason, there was not a special process to address the boxed warning with VANCO READY use at Infinium Pharmacy. However, on occasion the pharmacy does service a psychiatric

facility with younger patients, so particular care is taken when they receive vancomycin orders for those specific residents. Cerotti saw a great benefit in adding an alert related to the boxed warning for VANCO READY to the order-entry process for when the pharmacy services younger patients that could be pregnant or within child-bearing age. These additional steps taken help to ensure the safe implementation and use of the product.

Limitations to switching. There were some initial limitations to using the VANCO READY product, but these were resolved. When Infinium first implemented the product, there were not as many dosing strengths available. Now that all seven major adult vancomycin doses are available, this product is the go-to therapy, most commonly for osteomyelitis, lower respiratory tract infections, infective endocarditis, septicemia, and skin and soft tissue infections.

Changes and Processes

Easy switch. There were no organized discussions with management required to support the switch to VANCO READY. The infusion consultant pharmacist simply recommended and led the switch. Because the product had standard doses and could utilize the same infusion pumps, the process was quick and efficient and took very little time to implement (when it came to ordering, updating EMR, stocking, rolling out, etc.).

Fifteen-minute labeling process change. The only changes to the process for Infinium Pharmacy involved updating the premixed product sig codes (labeling) in the pharmacy's dispensing system to automatically populate the storage parameters, infusion rates, and stability outside of the overwrap. The new labeling process was then explained to staff. This process was simple, taking less than 15 minutes with pharmacy staff.

Long-term care facility implementation. The change was immediate upon receipt of the product. Infinium Pharmacy did not provide in-services to nursing staff. The product does not require activation, so outside of the labeling instructions and nursings' competence with the administration of any intravenous vancomycin formulation, further training was not necessary.

Conclusion

The product and supply costs between externally compounded product, bag-to-vial product, and room-temperature premixed product were all comparable for this pharmacy because of their lack of a clean room. The costs associated with credentialling and maintaining a cleanroom, compounding supplies, and pharmacy and/or nursing labor hours, were considered significant. Opportunities for error throughout the compounding and bag-to-vial activation of vancomycin were also high, and the opportunity to reduce those errors was a motivating factor when considering VANCO READY over compounding and bag-to-vial options. Because VANCO READY is premixed, and is ready to be infused, it may help mitigate the risks associated with compounding drugs.[2-5] Furthermore, the room-temperature premix is not only an excellent option for smaller pharmacies who do not have a certified cleanroom, but it also quickens the dispensing process for vancomycin, which is a frequently used therapy for residents in long-term care settings. For large and small sized pharmacies, this product is a great option to consider, especially for those pharmacies that supply first-dose vancomycin to nursing facilities utilizing emergency kits/automated dispensing cabinets. As a result, pharmacists and nurses can employ a vancomycin "system" that eases the labor-intensive burden of compounding, dispensing, and bag-to-vial activation. The benefits seen by our patients include improved medication safety, consistent product quality, and quicker turnaround times for new or updated vancomycin orders.

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VANCOMYCIN INJECTION, safely and effectively. See full prescribing information for VANCOMYCIN INJECTION.

VANCOMYCIN injection, for intravenous use
Initial U.S. Approval: 1958

RECENT MAJOR CHANGES

Boxed Warning	10/2021
Warnings and Precautions, Severe Dermatologic Reactions (5.5)	5/2021
Warnings and Precautions, Potential Risk of Exposure to Excipients During the First or Second Trimester of Pregnancy (5.1)	10/2021

WARNING: POTENTIAL RISK OF EXPOSURE TO EXCIPIENTS DURING THE FIRST OR SECOND TRIMESTER OF PREGNANCY

See full prescribing information for complete boxed warning.

If use of vancomycin is needed during the first or second trimester of pregnancy, use other available formulations of vancomycin. This formulation of vancomycin injection contains the excipients polyethylene glycol (PEG 400) and N-acetyl D-alanine (NADA), which resulted in fetal malformations in animal reproduction studies at dose exposures approximately 8 and 32 times, respectively, higher than the exposures at the human equivalent dose (5.1, 8.1).

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)

DOSAGE AND ADMINISTRATION

- Obtain a pregnancy test in females of reproductive potential prior to initiating treatment with Vancomycin Injection. *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1,8.3)]*
- Use this formulation of Vancomycin Injection only in patients who require the entire (500 mg, 750 mg, 1 g, 1.25 g, 1.5 g, 1.75 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, USP: Single-dose flexible bags containing 500 mg vancomycin in 100 mL, 750 mg vancomycin in 150 mL, 1 g vancomycin in 200 mL, 1.25 g vancomycin in 250 mL, 1.5 g vancomycin in 300 mL, 1.75 g vancomycin in 350 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)
- Severe Dermatologic Reactions: Discontinue Vancomycin Injection at the first appearance of skin rashes, mucosal lesions, or blisters. (5.5)
- *Clostridioides difficile*-Associated Diarrhea: Evaluate patients if diarrhea occurs. (5.6)
- Neutropenia: Periodically monitor leukocyte count. (5.8)
- Phlebitis: To reduce the risk of local irritation and phlebitis administer Vancomycin Injection by a secure intravenous route of administration. (5.9)
- 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. (5.10)

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)

See 17 for patient counselling information.

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