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ISMP Medication Error Report Analysis

Varizig Dilution Issue Reported

Prostin E2 Suppository Confused with Progesterone

FIRST Brand Oral Vancomycin Needs Improved Labeling

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These medication errors have occurred in health care facilities at least once. They will happen again—perhaps where you work. Through education and alertness of personnel and procedural safeguards, they can be avoided. You should consider publishing accounts of errors in your newsletters and/or presenting them at your inservice training programs.

Your assistance is required to continue this feature. The reports described here were received through the Institute for Safe Medication Practices (ISMP) Medication Errors Reporting Program. Any reports published by ISMP will be anonymous. Comments are also invited; the writers' names will be published if desired. ISMP may be contacted at the address shown below.

Errors, close calls, or hazardous conditions may be reported directly to ISMP through the ISMP Web site (www.ismp.org), by calling 800-FAIL-SAFE, or via e-mail at ismpinfo@ismp.org. ISMP guarantees the confidentiality and security of the information received and respects reporters' wishes as to the level of detail included in publications.

VARIZIG DILUTION ISSUE REPORTED

An issue came to our attention recently regarding varicella zoster immune globulin (*Varizig*), indicated for postexposure prophylaxis against chickenpox in high-risk individuals, such as children and adults who are immunocompromised. The product is available as a kit that contains a single vial of diluent along with a vial of 125 units of lyophilized powder (labeled as international units or IU, which ISMP deems an unsafe and unnecessary expression that is sometimes misread as IV). The diluent is packaged as a single-dose vial containing 8.5 mL. *Varizig* is approved in the United States for intramuscular (IM) use only but is approved in Canada for IM or intravenous (IV) use (**Figure 1**). According to the US label, only 1.25 mL of diluent is necessary for reconstitution of the 125 unit vial for IM use, resulting in a solution of 100 units per mL. In Canada where IV use is approved, 2.5 mL of diluent must be added to the vial.

Recently, in a US hospital emergency department (ED), a 5-year-old pediatric patient was to receive 125 units IM. However, a nurse misunderstood the instructions and used the entire volume of diluent (8.5 mL) to reconstitute the product. Rather than waste the dose, the nurse decided to divide the dose into two 3 mL injections and one 2.5 mL injection—for a total of 3 IM injections, which is bound to be traumatizing, particularly for a 5-year-old child. It is unclear why the instructions were misunderstood, but because only a fraction of the diluent (1.25 of the 8.5 mL) is necessary, it is likely that the packaging contributed to the error. We can also foresee a situation in which the entire diluent is used to reconstitute the powder and the practitioner assumes this provides the labeled 100 units per mL concentration, which would lead to a subtherapeutic dose.

The product is distributed in the United States by Emergent Biosolutions and manufactured by its subsidiary, Cangene Biopharma, in Canada. According to Emergent Biosolutions, the diluent vial presently contains 8.5 mL because higher doses were originally used in Canada and stability studies were conducted

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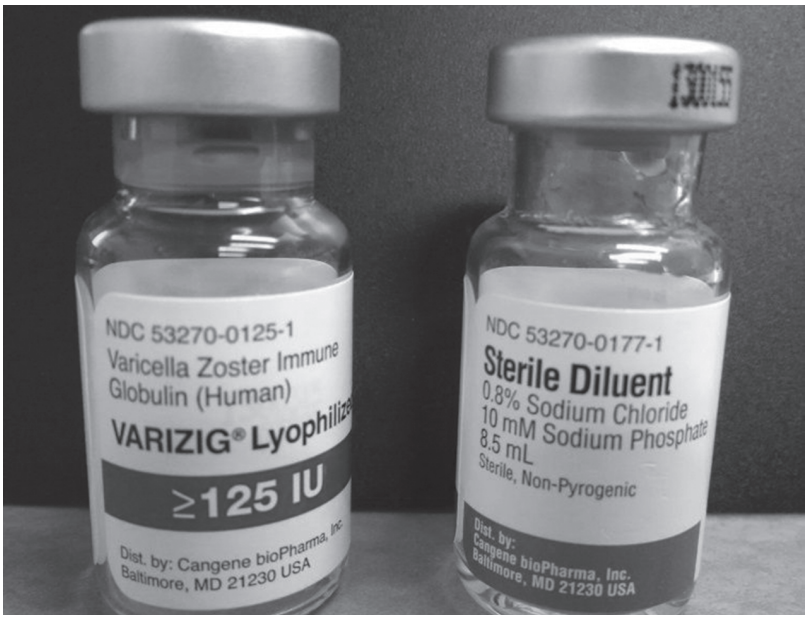

Figure 1. *Varizig* and sterile diluent container.

with larger diluent volumes. The company told us that Cangene has a new liquid form of the product under development that will not require reconstitution. The dosing for the new formulation is also weight-based and may require more than one vial according to a dosing chart in the package insert. For now, if you stock the lyophilized product, consider adding an auxiliary label that reminds practitioners to reconstitute with the volume listed in the labeling (1.25 mL per 125 unit vial, which provides 100 units per mL) and then to discard the remaining diluent.

We also had a pharmacist express concern regarding the amount of sodium phosphate administered based on the diluent vial label. The label states that it contains "10 mM" of sodium phosphate, which seems to be a high dose of sodium phosphate for treating hypophosphatemia. Don't confuse mM with mmol (as we did along with the reporter). Ten mM actually means 10 mmol per liter. Thus, the entire volume of diluent (8.5 mL) would provide 0.085 mmol of sodium phosphate, which is well below the maximum recommended dose of 0.36 mmol/kg (according to Lexicomp) whether given IV or IM.

PROSTIN E2 SUPPOSITORY CONFUSED WITH PROGESTERONE

A 26-year-old woman who was 27.5 weeks pregnant had been receiving vaginal progesterone due to cervical shortening. Such a condition may be due to normal biologic variance or may result from physiological factors during pregnancy. In either case, it is a risk factor for preterm labor in both low-and high-risk pregnancies. In this case, the patient came to the obstetrical clinic for 23-hour fetal monitoring, which revealed asymptomatic uterine contractions. Progesterone is sometimes used in such cases (www.ismp.org/sc?id=404), so the patient was transferred to a labor and delivery (L&D) unit and prescribed a vaginal progesterone suppository as prophylaxis.

Over the next few hours, the patient became increasingly ill and complained of back pain and abdominal cramping. Unfortunately, staff initially dismissed her symptoms as "something she ate" or "nervousness," and she was given sedatives. However, the symptoms continued and she eventually delivered a 1.1 kg baby boy. The infant was rushed to the neonatal intensive care unit (NICU) where he remained stable but in guarded condition. The mother was later discharged from the hospital, but the baby remained in NICU.

Upon further follow-up, an L&D nurse realized that an error had been made. She accidentally gave the patient a *Prostin E2* (dinoprostone) vaginal suppository instead of the prescribed progesterone. Dinoprostone vaginal suppositories are indicated for evacuation of the uterine contents in the management of missed abortion or intrauterine fetal death (IUFD). They are also used for termination of pregnancy and benign hydatidiform mole. The

medications were both available in the L&D drug storage area.

In L&D, the standard procedure for drug administration did not include barcode scanning of the patient identification bracelet and medication against the medication record because nurses often had to "move quickly." Thus, an opportunity to prevent the error was lost. If available, barcode scanning should always be used except in emergencies.

Remove the *Prostin E2* suppository from stock in patient care areas and add a warning on the screens of pharmacy and electronic prescribing systems that *Prostin E2* is indicated for IUFD, uterine evacuation, and termination of pregnancy only.

FIRST BRAND ORAL VANCOMYCIN NEEDS IMPROVED LABELING

With the limited availability of oral vancomycin products in recent months, pharmacists have sought alternatives, such as reconstitution of parenteral vials of sterile powder for use as an oral solution and then repackaging the solution prior to dispensing. Recently, a more convenient alternative became available. In spring of 2014, CutisPharma launched unit-of-use compounding kits for vancomycin oral solution under the *FIRST* trademark. The kits contain a bottle of vancomycin powder along with a bottle of grape-flavored diluent. Both 25 mg per mL and 50 mg per mL concentrations are available after reconstitution. Container sizes include 150 mL, 210 mL (50 mg/mL only), and 300 mL. Prior to use, the contents of each bottle must be properly reconstituted.

Although this product is convenient to use, we have received reports about the product not being clearly labeled. One of the issues is that the diluent container, which has no vancomycin, and the powder have "vancomycin 25" or "vancomycin 50" listed at the top of the label (**Figure 2**). The fear is that someone unfamiliar with the product might see the diluent as a bottle of active drug, especially when the containers have been removed from the carton. For example, this product might be stored in an automated dispensing cabinet (ADC) on patient care units in a hospital without 24-hour pharmacy service so nurses can access the product.

Administration of the diluent alone has happened in the past with other oral antibiotics that require reconstitution with a special diluent. A similar situation occurred with *Cipro* oral suspension (ciprofloxacin), which is supplied as an active antibiotic powder along with a diluent. However, at one time, both containers were labeled "Cipro Oral Suspension." This sometimes

Figure 2. *FIRST* brand vancomycin compounding kit.

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D of 86.2 pg/mL (reference range, 25-65 pg/mL), aldosterone 1.8 ng/dL (reference range,4.5-35.4 ng/dL), renin 1.7 µg/L/h (reference range,0.8-5.8 µg/L/h), and a random urine magnesium of 14 mg/dL (reference range, female ≥40 years of age, 0.4-15 mg/dL).

The authors point out that proton pump inhibitors (PPIs) can induce hypomagnesemia, which can lead to seizures, arrhythmias, hypotension, tetany, and death. Magnesium is excreted via the renal and gastrointestinal route, so the prime culprit in PPI-induced hypomagnesemia is impaired intestinal absorption of magnesium. The authors recommend that in patients with gastrointestinal malabsorption of magnesium, H_2 blockers should be the first-line therapy; if PPI therapy is required, then close monitoring of magnesium is necessary especially in cardiac patients who might have a propensity for arrhythmia.

Nand B, Bhagat M. Serious and commonly overlooked side effect of prolonged use of PPI. *Am J Med*. 2014;127(9):e5. ■

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led to the diluent being identified as a ready-to-use product, and it was dispensed without reconstituting the actual antibiotic. At the time, ISMP called upon the US Food and Drug Administration (FDA) and the manufacturer to improve label clarity, and the diluent container labels were then revised to state, "diluent for Cipro Oral Suspension." Similarly, the new vancomycin product diluent bottle should be prominently labeled, "diluent for vancomycin 25" or "diluent for vancomycin 50."

We also received reports in which the powder alone was dispensed without dilution for oral antibiotic products. This can happen with this product, because the powder container is marked with an icon that states, "Oral Solution." Another issue with this product is that the bottle of vancomycin powder, which acts as the dispensing container after reconstitution, is not prominently labeled with the expected final concentration or the total volume after reconstitution. This information may not be available unless the bottle happens to be relabeled with that information once reconstituted.

The powder container should state, "Vancomycin 25 Powder—Must be Diluted." Until this change is made by the company, hospitals and pharmacies using this product are advised to label containers appropriately so the grape diluent is not administered as the drug itself or the powder is not administered or dispensed without dilution. We also recommend labeling the reconstituted powder containers with the final concentration per mL and total volume, along with the notation, "Reconstitution Completed."

We have contacted both FDA and CutisPharma to request improvements to the way the product carton and containers are labeled. ■