# ISMP

# Nurse Advise ERR®

Educating the Healthcare Community About Safe Medication Practices

# Paralyzed by mistakes Reassess the safety of neuromuscular blockers in your facility

Neuromuscular blocking agents are high-alert medications because of their well-documented history of causing catastrophic injuries or death when HIGH-ALERT used in error. These drugs are used during endotracheal intubation, during surgery of intubated patients, and to facilitate mechanical ventilation of critically ill patients. However, neuromuscular blockers have been inadvertently administered to both adult and pediatric patients who were not receiving proper ventilatory support. Because neuromuscular blockers paralyze the muscles that are necessary for breathing, some patients have died or sustained serious, permanent injuries if the paralysis was not witnessed by a practitioner who could intervene.

After a patient receives a neuromuscular blocker, progressive paralysis develops, initially affecting the small muscle groups such as the face and hands, then moving to larger muscle groups in the extremities and torso until all muscle groups are paralyzed and respiration ceases. However, full consciousness remains intact, and patients can experience intense fear when they can no longer breathe. They can also sense pain. The experience can be horrific for patients and can lead to psychological trauma, including post-traumatic stress disorder.<sup>1</sup>

The ISMP National Medication Errors Reporting Program (ISMP MERP) has received well over 100 reports of errors involving neuromuscular blockers. However, the true incidence of injuries from erroneous administration of neuromuscular blockers is much higher than reflected in our error-reporting program. While some errors have occurred during anesthesia in the operating room (OR), many have taken place outside this setting, in emergency departments (EDs), interventional radiology departments, intensive care units (ICUs), and other medical, surgical, and psychiatric units.

The most common type of error with neuromuscular blockers appears to be administration of the wrong drug. A 2009 analysis of 154 events over a 5-year period showed that a neuromuscular blocker was not the intended drug in approximately half of all wrong drug errors.<sup>2</sup> Practitioners thought they were administering a different drug, so patients may not have been supported with mechanical ventilation. More than 80% of these wrong-drug errors reached the patient, and approximately a quarter resulted in patient harm—a rate significantly higher when compared to less than 1% of events causing harm with all other wrong-drug errors during the same study period.<sup>2</sup>

Errors with neuromuscular blockers can be attributed to one or more common causes. The following are some examples.

# Look-alike packaging and labeling

An ED nurse administered pancuronium instead of influenza vaccine to several patients. The vials were the same size, and the labels were quite similar. The look-alike vials had been stored next to each other in the refrigerator. The patients experienced dyspnea and respiratory depression but, fortunately, sustained no permanent injuries. continued on page 2—Neuromuscular blockers >

#### 19th Annual ISMP Cheers Awards

Each year, ISMP celebrates individuals and organizations that have set a standard of excellence in the prevention of medication errors during the previous 12 months. Nominations for this year's **Cheers Awards** will be accepted through **September 9**. ISMP accepts outside nominations, including self-nominations. The prestigious awards spotlight efforts from all healthcare disciplines, including nursing, medicine, and pharmacy, and winners have represented all practice areas, including acute care, long-term care, home care, and community pharmacy settings. To submit a nomination, please visit: www.ismp.org/sc?id=1777.

# **SAFETY** wires

Safer drug storage. We like an idea for drug storage that we just saw in a Health Care Logistics advertisement. The company sells what they refer to as "vial grippers" that help to "neatly organize medication vials lying flat inside a code cart box or drawer and keep labels facing up so they are easy to read, which may help prevent errors when obtaining medications" (Figure 1). Without doubt, one of the most common errors reported to the ISMP National Medication Errors Reporting



**Figure 1.** "Vial grippers" (Health Care Logistics) can help keep the labels on vials facing forward. (Labels are facing away in the photo but should be facing forward to improve vial identification.)

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Supported by educational grants from Baxter, Novartis, and Fresenius Kabi

Baxter

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Several practitioners reported concern regarding the similarity of flumazenil 0.5 mg/ 5 mL and vecuronium 10 mg vials from NOVAPLUS once the different colored caps

have been removed (**Figure 1**, left two vials). Both may be stored in procedural areas, increasing the risk of a mix-up.

Similar colors and label graphics contribute to Mylan's vecuronium 20 mg and vancomycin 1 g vials looking alike (**Figure 1**, right two vials), especially with the caps removed. Both contain white lyophilized powder that requires reconstitution.



Figure 1. Once the caps are removed, these vials look very similar. However, a mix-up could be catastrophic.

# **Look-alike drug names**

**NARCAN** (naloxone) and **NORCURON** (vecuronium) have been confused with written and verbal orders. In one case, a nurse transcribed a verbal order for Narcan correctly, but a pharmacist misread the order and dispensed Norcuron. The nurse thought Norcuron was the generic name for Narcan and administered it. In another case, a physician prescribed Narcan but an ICU nurse did not recognize the drug on the automated dispensing cabinet (ADC) screen because it was listed by its generic name. She intended to ask a coworker for Narcan's generic name, but she mistakenly asked for the generic name of Norcuron. She then removed vecuronium from the ADC and administered it. The patient arrested, was resuscitated, placed on a ventilator, and later fully recovered.

# Drug administration after extubation

A ventilated ICU patient was receiving vecuronium and a potassium chloride infusion. After the patient was extubated, an infusion bag containing vecuronium remained in the room and was mistaken as a potassium chloride infusion. Soon after the medication was started, the patient arrested, requiring intubation and ventilation for 6 more hours.

# Unlabeled and mislabeled syringes

Prefilled syringes of saline flushes were not available in the ED, so nurses prepared a supply each day from multiple-dose vials. Vecuronium had recently been prepared for a trauma patient in the ED, but it was not used. The syringe was not labeled and was inadvertently placed with the saline flush syringes. The syringe containing vecuronium was later used to flush the IV line of a 3-year-old child. The child became flaccid and stopped breathing. She was quickly intubated and ventilated, so permanent harm was averted.

An anesthesiologist was interrupted while preparing syringes of midazolam and rocuronium.<sup>3</sup> When he returned, he administered the contents of one syringe to a patient in the holding area, believing it contained midazolam. He was again called away, and when he returned, the patient was unresponsive. The patient was intubated and given a reversal agent, and surgery was postponed. It was later determined that the anesthesiologist had administered the syringe containing rocuronium.

A pharmacy prepared batches of succinylcholine and e**PHED**rine in ready-to-use syringes for the labor and delivery unit. The technician prepared both correctly and placed them in a divided bin to be checked. Either the labels were placed in the wrong compartments, or they were placed in the correct compartments but were applied to the wrong syringes. A dose of succinylcholine was administered IV instead of e**PHED**rine to treat hypotension. The patient experienced respiratory arrest but was resuscitated successfully.

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Program (ISMP MERP) is a mix-up between look-alike vials placed into or removed in error from the same storage drawer or bin.

We frequently identify problem pairs of drug vials that we think would benefit from organized storage with labels facing forward, rather than just adding them loosely to the drawer where they may be turned haphazardly. We thought it was worth calling these "vial grippers" to your attention. However, we would not recommend using the color of the grippers as a means of color-coding different medicationsperhaps the same color grippers should be purchased and used in an organization. Additional information on the "vial grippers" can be found at: www.ismp.org/sc?id=1739.

Aggrastat-argatroban mix-ups. We are aware of three mix-ups in two hospitals that resulted in the pharmacy dispensing infusions of AGGRASTAT (tirofiban) instead of argatroban. Both of these high-alert medications are available in 250 mL premixed bags, although Aggrastat is 12.5 mg/250 mL (a premixed 5 mg per 100 mL is also available), and argatroban is 250 mg/250 mL. In two of the cases, the error reached the patient and was not discovered until the next dose was due. Bedside barcode scanning was in place at one of the hospitals, but pharmacy printed and affixed a patient label with a barcode for argatroban on an Aggrastat bag. A nurse scanned the pharmacy label, which confirmed that argatroban was printed on the pharmacy label, when the drug in the bag was actually Aggrastat.

Part of the problem was that these drugs were stored near one another; they have since been moved so they are no longer side-by-side. Also, the pharmacy no longer prints a barcode on labels for Aggrastat or argatroban. They have the nurse scan the actual manufacturer's barcode on the bag label. The hospital also believes that look-alike drug names played a role in the mix-up, so they've started using their own tall man letters continued on page 3—*SAFETY* wires >

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#### **5** Unsafe storage

Atracurium was administered instead of hepatitis B vaccine to several infants, who developed respiratory distress. One infant sustained permanent injury and another died. Neuromuscular blockers had never been available as unit stock in the nursery. An anesthesiologist from a nearby OR had placed the atracurium vial in the nursery refrigerator near look-alike vaccine vials. Similar mix-ups with vaccines continue to occur.<sup>4</sup>

In a pediatric ICU, a respiratory therapist obtained what he thought was a vial of sterile water to prepare a nebulizer treatment. As he was piercing the stopper, he noticed that he had accidentally grabbed a vial of atracurium that someone had inadvertently returned to a respiratory box in the refrigerator.

#### Orders entered into wrong electronic health record

A medical resident electronically prescribed vecuronium for the wrong patient with a similar name, who was located on a medical unit. The correct patient was ventilated and in the ICU. The pharmacist and technician did not question the infusion for a patient on a medical unit. An independent double check was carried out by two nurses before administration, but neither nurse was aware that the patient required ventilation with this drug.

#### **Knowledge deficit about drug action and required ventilation**

An ED physician gave a verbal order for a trauma patient to receive vecuronium and midazolam, which were administered prior to intubation. He then mistakenly entered electronic orders for these medications into another patient's record. An ED nurse administered the medications to the patient without recognizing that vecuronium would paralyze the respiratory muscles. After she left the room, the patient arrested. The ED team responded, but the patient could not be resuscitated.

# Syringe swaps

Succinylcholine was inadvertently administered instead of fenta**NYL** prior to the induction of anesthesia.<sup>5</sup> The anesthetist had drawn up both drugs into 2 mL syringes, and had applied a blank red and black label on the succinylcholine syringe and a manufacturer-supplied label to the fenta**NYL** syringe, which was also red and black a label color in anesthesia reserved for neuromuscular blockers. The anesthetist picked up the succinylcholine syringe, believing it contained fenta**NYL** based on its position on the table.

A patient became unresponsive in the holding area after IV administration of cisatracurium instead of midazolam. The patient was ventilated and the surgery proceeded. Two additional syringe swaps involving cisatracurium outside the OR were reported.<sup>3,6</sup>

# Reversal agent not available

Several practitioners have reported that reversal agents (i.e., neostigmine, sugammadex) for neuromuscular blockers have not been available when needed in the OR and elsewhere. One reporter said the reversal agents were stored in a locked cabinet and were not accessible.

# <u>A</u> Residual drug in tubing

In a post-anesthesia care unit (PACU), a nurse administered a dose of **HYDRO**morphone through an IV line in the patient's left arm. The IV line in the patient's right arm was clamped, so the nurse opened the line and flushed it. About 2 minutes later, the patient stopped moving and breathing, and his oxygen saturation fell to 40%. Anesthesia was called, and the problem was thought to be caused by continued on page 4—Neuromuscular blockers >

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for these drugs—"aggra**STAT**" and "ar-**GATRO**ban." Incidentally, in one of the mix-ups, pharmacy had a process in place to scan the manufacturers' barcodes before dispensing, but two staff members skipped this step, and the system still allowed the drug to be dispensed from the pharmacy. A hard stop requirement for scanning the product is needed to address this type of omission. Finally, a pop-up warning at the point of administration now alerts the nurse to visually verify that he/she is hanging the correct drug—argatroban or Aggrastat.

#### ) Mistake in argatroban dosing table.

A few months ago, a physician stopped by the pharmacy with a pharmacy-dispensed carton of argatroban for a coronary artery bypass graft (CABG) patient with heparin-induced thrombocytopenia. The physician pulled out the package insert to ask the pharmacist about one of the tables, which had weight-based dosing rates listed in mg/min (minute). He wanted to be sure that he wasn't misunderstanding the dosing. The pharmacist double checked the math in that table and realized that the mg/min dosing rates would cause a 1,000-fold overdose. The values should have been stated as mcg/min. The rate in mL/hr was correct if diluted per the manufacturer recommendations. Figure 1 shows the part of Table 2 in the package insert that lists mg/min in error.

Infusion Dosing For ACT 300-450 seconds 25 mcg/kg/min	
Continuous Infusion Dose (mg/min)	Continuous Infusion Rate (mL/hr)
1250	75
1500	90
1750	105
2000	120
2250	135
2500	150
2750	165
3000	180
3250	195
3500	210

Figure 1. Argatroban continuous infusion dose should be mcg per minute, not mg per minute.

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Also partially supported by an educational grant from **NEOMED** 

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flushing the remaining rocuronium in the IV tubing into the patient. Neostigmine was administered for blockade reversal.

#### **Dose or rate confusion**

Mental mix-ups have led to numerous dosing errors. For example, rocuronium was infused at the rate intended for cisatracurium, and several patients received the wrong dose of rocuronium because the physician dosed it in mcg/kg/hour, not mcg/kg/minute.

Serious adverse events continue to occur with neuromuscular blockers when they are used without adequate safeguards. Although the causes are varied, many of the most harmful or fatal errors involve the accidental administration of a neuromuscular blocker when another drug is intended. Thus, adherence to proper ordering, storage, selection, preparation, and administration is paramount. Neuromuscular blockers are also a focus of Best Practice 7 in the ISMP **2016-2017 Targeted Medication Safety Best Practices for Hospitals**, which aims to promote safe storage of neuromuscular blockers.<sup>7</sup>To reduce the risk of harm from neuromuscular blockers, consider the following recommendations. The **Primary Recommendations** should be given the highest priority for action by hospitals and surgery centers. The **Secondary Recommendations** are also very important but address the common causes of medication errors that are not necessarily unique to neuromuscular blockers.

#### Primary Recommendations

**Assess labeling and packaging.** Require a medication safety officer (MSO) and an anesthesia staff member to evaluate any new neuromuscular blocker's packaging and labeling prior to procurement, and introduce auxiliary label enhancements and education, if necessary, before distribution.<sup>6</sup> Use brands of neuromuscular blockers that clearly differentiate the vials from other products via warnings on the label, vial cap, and metal ferrule around the rubber stopper. (All manufacturers of these agents are required to provide cautionary labeling. The development of a universal symbol for neuromuscular blockers remains to be determined.<sup>8</sup>) Avoid ampuls, which have small, hard-to-read labels.

**Standardize prescribing.** Outside the OR or procedural areas, orders for neuromuscular blockers should only be part of an intubation protocol, or an order set to maintain a specific level of paralysis while the patient is mechanically ventilated. Do not accept neuromuscular blocker orders that specify to "use as needed for agitation." Include the need for ventilation support during and after administration, and automatically discontinue these agents in electronic records after extubation. Prohibit orders to "resume the same medications" upon patient transfer.

**Use clear terminology.** Always refer to these drugs as "neuromuscular blockers" or "paralyzing agents." Never call them "muscle relaxants."

**Build computer reminders.** Build alerts in the computer system to verify the patient's location when neuromuscular blocker orders are being prescribed or entered/verified by pharmacy. If the patient is not in a critical care unit, ED, OR, or invasive procedure area, prescribers should verify that they are entering the order into the correct patient profile, and pharmacists should question the order and verify ventilatory assistance before dispensing the drug. Also, provide a cautionary message on ADC screens that requires staff to acknowledge that the patient is, or immediately will be, receiving ventilator support when a neuromuscular blocker is selected for removal.

Limit access. Eliminate the storage of neuromuscular blockers in areas of the hoscontinued on page 5—Neuromuscular blockers >

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When we heard about this issue, we looked at every package insert from other manufacturers of this product (Sandoz, Teva, GSK, Fresenius, West-Ward, and Eagle) and found the same error, except for Par Pharmaceutical. (All the package inserts on DailyMed have since been updated.) An error in magnitude of 1,000 was overlooked by multiple drug companies, drug package insert reviewers, the US Food and Drug Administration (FDA) approval channels, and many others who missed the error. An independent check of the dosing tables and their calculations might have identified the error immediately. It's an important lesson, because the same thing could easily happen at a hospital when developing order sets, forms, tables, and so on. Please check to make sure this table was not copied into an order set or is otherwise being used to guide therapy. We thank the doctor and pharmacist who picked up this error AND reported it. You showed us the importance of speaking up about the errors you find.

Restasis mixed up with Refresh Celluvisc. We have received several re-

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ports of events involving Allergan's RESTASIS (cycloSPORINE ophthalmic emulsion) being confused with their over-the-counter REFRESH CELLUVISC (carboxymethylcellulose) lubricant eye gel. In one case, a pharmacy technician prepared a bag of Restasis instead of Refresh Celluvisc for a patient, although the error was discovered by a pharmacist before the product was dispensed. Another close call occurred in a hospital pharmacy where Restasis was mixed in with a number of Refresh Celluvisc plastic ampuls. This error was also identified before dispensing took place.

In yet a third case, a medication error occurred when Restasis was accidently returned to the Refresh Celluvisc bin in the pharmacy and later stocked in an operating room automated dispensing cabinet (ADC). A continued on page 5—SAFETY wires >

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pital where they are not needed.<sup>7</sup> Allow unit stock only in the OR, ED, and critical care units where patients can be properly ventilated and monitored. Consider limiting the number of neuromuscular blockers on formulary, and store these agents separately from pharmacy stock when possible. Regularly review these storage areas, both inside and outside of the pharmacy, including agents that require refrigeration, and consider the potential for mix-ups. Limiting access to these products is a strong deterrent to inadvertent use.

**Segregate storage.** Segregate, sequester, and differentiate all neuromuscular blockers from other medications, wherever they are stored in the organization.<sup>7</sup> In areas where they are needed, place neuromuscular blockers in a lidded box or in a rapid sequence intubation (RSI) kit. One option for storage is a highly visible redorange container available commercially (www.ismp.org/sc?id=458). If neuromuscular blockers must be stored in ADCs, keep them in separate lidded pockets, away from other drugs. Organize anesthesia carts and trays to avoid placing look-alike vials, syringes, or bags next to each other, and display the labels so they are readily visible.

Affix warning labels. Place auxiliary labels on all storage bins and final medication containers (e.g., vials, syringes, IV bags) of neuromuscular blockers that state: "WARNING: PARALYZING AGENT–CAUSES RESPIRATORY ARREST," to clearly communicate that respiratory paralysis will occur and ventilation is required. The warning labels should not cover important label information. For infusions, one hospital system places a warning on a port tag that will be seen by nurses when they spike the bag to attach tubing. The use of shrink-wrap sleeves with cautionary labeling placed over vials is questionable because they make all vials look alike.

**Dispense from pharmacy.** Never dispense a neuromuscular blocker to a unit that cannot support mechanical ventilation. For nonurgent doses in the OR or ED, and continuous infusions in the ICU, dispense neuromuscular blockers from the pharmacy in the most ready-to-use form. The Anesthesia Patient Safety Foundation recommends the use of either commercially available, outsourced, or pharmacy prepared and labeled, prefilled syringes and infusions of neuromuscular blockers (and other anesthesia drugs), rather than unit based, self-prepared syringes or infusions.<sup>9</sup> Properly labeled, prefilled syringes have the potential to improve system safety, reduce syringe swaps, and enhance work efficiency.<sup>10</sup>

**Verify neuromuscular blockers.** Remind practitioners that reading labels is the first defense to avoid an error. Equally important given human fallibility, implement point-of-care barcode scanning to verify neuromuscular blockers and patients before administration. In the OR and procedural areas, if barcode scanning is not undertaken, consider alternative verification systems including speakers and touch screens that provide automatic auditory and visual verification of drugs and important alerts prior to administration.<sup>11,12</sup>

**Use smart infusion pumps.** Administer all neuromuscular blocker infusions via a programmable smart infusion pump utilizing dose error-reduction software. Smart infusion pumps should be programmed to allow selection of a neuromuscular blocker infusion only in patient care areas capable of caring for ventilated patients receiving such agents. When a neuromuscular blocker is selected in units where ventilation is possible, a clinical advisory warning should note that the drug paralyzes the respiratory muscles, and the nurse must confirm that the patient is on mechanical ventilation. The flow rate of infusions of neuromuscular blockers should be presented and entered into the pump using the same standard dosing units prescribers use (e.g., mcg/kg/minute vs. mcg/kg/hour).

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nurse then removed what she thought was a Refresh Celluvisc ampul from the ADC, tried unsuccessfully to scan the product, and then administered it to the patient. The error was discovered while investigating why these unit-dosed ophthalmic medications did not have a barcode on them, making the products themselves unscannable. For now, pharmacy must print labels with barcodes and place them on these products for nurses to scan prior to administration. When this is done, we recommend placing the label on either end of the container, away from the solution.

Errors can still happen when barcode labels are placed on the container by pharmacy. In the case just mentioned, the barcode label for Refresh Celluvisc was incorrectly placed on the Restasis product by pharmacy. Not only is the packaging identical but the text on the unit dose package also looks similar (**Figure 1**). We have asked both the US Food and Drug Administration (FDA) and the manufacturer to look into the situation. The FDA barcode



**Figure 1.** Plastic ampuls of Restasis (top) and Refresh Celluvisc (bottom) can be easily mixed up.

rule (www.ismp.org/sc?id=1705) exempts low-density polyethylene form fill and seal containers that are not packaged with an overwrap from needing a barcode. (FDA is in the process of revising the barcode rule, although we have no further information.) A mix-up between these two products could lead to omission of cyclo**SPORINE** or inappropriate administration.

Liquid megestrol-metoclopramide mix-up. A hospitalized patient was scheduled to receive megestrol 400 mg/10 mL oral suspension, but the continued on page 6—SAFETY wires >

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# Secondary Recommendations

**Require proper labeling.** Promote accurate labeling of all infusions and syringes containing neuromuscular blockers both in the OR and in patient care locations outside the OR. (When possible, ready-to-use syringes and bags should be provided.)

**Provide access to reversal agents.** Ensure all appropriate reversal agents for neuromuscular blockade are available to qualified staff who might need them in an emergency. In protocols, identify who is permitted to administer the reversal agent in an emergency and provide readily available instructions for administration.<sup>7</sup>

**Flush the line.** If a neuromuscular blocker has been administered via infusion, all of the residual drug should be flushed from the IV line (source container removed or IV push flushed through the line) or the line should be changed or discontinued prior to extubation.

**Timely dispensing and prompt removal.** Pharmacy should practice just-intime dispensing of neuromuscular products when possible to avoid unnecessary access to these products before use. When the drugs are no longer needed, place unused vials and bags of neuromuscular blockers in a sequestered bin for return to the pharmacy. Unused patient-specific doses in syringes should be destroyed/discarded after the patient has been extubated or the drug has been discontinued.

**Increase awareness.** Educate staff about the risk of serious errors with these high-alert drugs. Provide staff with a list of both generic and brand names for all neuromuscular blockers available at your location, and include usual dosages and any special guidelines associated with preparation, distribution, administration, and monitoring. Also use the information above to assess your safety practices.

**Verify competency.** Establish a formal training program and competency verification process for practitioners involved in preparing, dispensing, and administering neuromuscular blockers.<sup>3</sup> These drugs should only be administered by staff with experience in maintaining an adequate airway and respiratory support, and only in units where intubation and respiratory support can be provided.

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automated dispensing cabinet (ADC) was incorrectly stocked with metoclopramide 10 mg/10 mL oral solution. Both products are distributed by Pharmaceutical Associates. The nurse retrieving the medication for her patient recognized the stocking error and informed the pharmacy. Related to the dispensing error, megestrol and metoclopramide oral liquids are stored in the pharmacy in bins that are right next to one another. Also, both medications deliver 10 mL and are available in very similar dosing cups, with



Figure 1. These two containers look alike and could be easily mixed up.

blue fonts and crowded labels that can contribute to a medication mix-up (**Figure 1**). The hospital told us that it is investigating alternative manufacturers to allow for a different package design to help distinguish each medication. Meanwhile, the hospital is no longer storing these near one another, and it has just begun implementation of barcode scanning in the pharmacy and at the bedside.

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