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Acute Care ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Paralyzed by mistakes

Reassess the safety of neuromuscular blockers in your facility

HIGH-ALERT

Problem: Neuromuscular blocking agents are high-alert medications because of their well-documented history of causing catastrophic injuries or death when used in error. These drugs are used during tracheal 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 assistance. 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.[1]

The ISMP National Medication Errors Reporting Program (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.[2] 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.[2]

Errors with neuromuscular blockers can be attributed to one or more common causes. The following provides a sampling of the causes of errors with examples.

1 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.

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A liquid dose cup you can read. Comar has begun distribution of mL-only liquid dose cups with an easy-to-read, printed scale. These are being distributed by Medi-Dose (www.ismp.org/sc?id=1749) and are available in three capacities: 20, 30, and 60 mL. Previous dosage cups we have seen have had embossed scales that were difficult to read or displayed both mL and teaspoonful amounts. We

Figure 1. A mL-only dosage cup with printed scale.

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20-year anniversary of this newsletter. The *ISMP Medication Safety Alert!* began publication on January 15, 1996. Now in its 20th year, we are highlighting some of the significant ISMP patient safety milestones—small snippets of articles or safety briefs we wrote so many years ago that are memorable, humorous, or still newsworthy.

A glimpse down memory lane

April 24, 1996 newsletter:

Be ready for accidental IV potassium overdoses

By 1996, ISMP was aware of multiple deaths and patient injuries that had been associated with accidental intravenous administration of concentrated potassium chloride injection prior to dilution. The drug was inadvertently given as a direct intravenous (IV) push injection or erroneously used as a diluent to prepare sterile antibiotic powders, then injected by direct IV

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*Several practitioners reported concern regarding the similarity of vials of flumazenil 0.5 mg/5 mL and vecuronium 10 mg from NOVAPLUS once the different colored caps have been removed (**Figure 1**, left). Both may be stored in procedural areas, increasing the risk of a mix-up.*

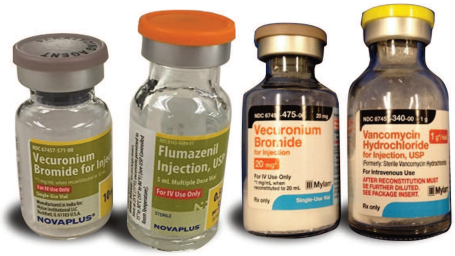

Figure 1. Once the caps are removed, these vials look very similar. However, a mix-up could be catastrophic.

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

2 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 and placed on a ventilator, and later fully recovered.*

3 Unsafe mnemonics

During pharmacy entry of an order for an infusion of cisplatin, the mnemonic computer rule after entering "cis" completed the drug field name with cisatracurium, generating a label for the neuromuscular blocker, which was prepared and dispensed.[3]

4 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.

5 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.[3] 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*

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push. Some of the incidents were associated with look-alike vials of potassium chloride and sodium chloride injection. It was very common to find potassium chloride vials on nursing units in nearly every US hospital. By 1987, ISMP had already convened a national meeting about potassium chloride deaths that helped influence the US Pharmacopeia (USP) and US Food and Drug Administration (FDA) to require vials of potassium chloride concentrate injection to have black caps, closures, and warning statements to prevent mix-ups with other parenteral drugs. Nevertheless, potassium chloride vials remained on nursing units, and unsafe practices, such as not labeling syringes of potassium chloride intended for IV admixture preparation, continued to contribute to fatalities.

In March 1995, ISMP sent a nationwide mailing to US hospitals that strongly recommended the removal of vials of potassium chloride concentrate for injection from patient care areas. On April 24, 1996, the *ISMP Medication Safety Alert!* included two potassium chloride overdoses in which nurses thought they were flushing an IV catheter with sodium chloride but inadvertently instilled potassium chloride. The March 1995 alert was highlighted along with a strong recommendation that, if potassium chloride concentrate continued to be stored in patient care areas, physicians and nurses must know how to immediately treat acute hyperkalemia caused by accidental injection of concentrated potassium chloride.

Two years later in 1998, in the first *Sentinel Event Alert* (www.ismp.org/sc?id=1729), The Joint Commission (TJC) asked hospitals to consider the recommendation that ISMP had made earlier. Later, in drafting the inaugural *National Patient Safety Goals*, TJC required hospitals to remove potassium chloride concentrate and other concentrated electrolytes from all patient care units outside of the pharmacy. Since that change, only one case of accidental IV push potassium chloride is known by us to have occurred in the US, in a nonaccredited hospital, in 2007.

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*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.*

6 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.[4]

In a pediatric ICU, a respiratory therapist obtained what he thought was a sterile water vial 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.

7 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 medical unit patient. 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.

8 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.

9 Syringe swaps

*Succinylcholine was inadvertently administered instead of fenta**NYL** prior to the induction of anesthesia.[5] 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.[3,6]

10 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 in a locked cabinet and not accessible.

11 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*

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have always called for the elimination of teaspoons, tablespoons, and drams on devices used for measuring liquid doses of medication. We are glad to see manufacturers are finally providing mL-only devices.

Misuse of new insulin strengths. We certainly have important education to accomplish with patients and health professionals regarding the new higher concentration insulin products that are available only in a pen, including U-300 **TOUJEO** (insulin glargine), U-200 **TRESIBA** (insulin degludec), and U-200 **HUMALOG** (insulin lispro). U-500 insulin is also available in a pen (**HUMULIN**), although vials remain on the market. Patients may not understand proper dosing and dose measurement with these higher concentrations of insulin products.

A patient who was previously using **LANTUS** (insulin glargine) U-100 was switched to Toujeo U-300. He was given pen needles to use with Toujeo, but at home, he decided to use the insulin pen cartridge as a vial. He drew up a dose with a leftover U-100 syringe, filling it to the 100 unit mark, the same daily Lantus dose he had been taking. This resulted in a dose of 300 units of Toujeo, which led to hypoglycemia requiring hospital admission.

Although the safety of using pen cartridges as a vial is questionable, health professionals who administer insulin have also used insulin pen cartridges as vials, sometimes even with hospital authorization (www.ismp.org/sc?id=1748). Using a U-100 syringe to measure higher concentrations of insulin could lead to a serious overdose, as in the above case.

With U-500, not only is there a risk of an overdose, but underdosing is also possible. In the past, many patients using vials of U-500 insulin measured their dose with a U-100 syringe but used the syringe scale to measure only 20% of the actual dose. For example, 40 units on the U-100 syringe scale is 200 units of U-500 insulin. If patients now use the new U-500 pen and dial only the number of units they previously measured (40 units), the patient would receive only one-fifth of the prescribed dose. With

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

12 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.

Safe Practice Recommendations: 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.[7] 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.[6] 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.[8])* 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 on a ventilator only. Do not accept neuromuscular blocker orders for "use as needed for agitation." Include the need for ventilation support during and after administration and *automatic* discontinuation of these agents in electronic records after extubation and removal from a ventilator. Completely disallow 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. If possible, establish computerized cross-checking of the patient's location when entering neuromuscular blocker orders (as with other drugs limited to administration on a specific unit). Cautionary messages may also appear on ADC screens.

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the various high concentration insulin products now available in pens, it is important to warn both patients and health professionals about these new risks.

Don't expect RFID stock systems to be perfect. A hospital that started using radiofrequency identification (RFID) technology to refill various emergency kits (e.g., anesthesia, rapid sequence intubation, stroke) told us about some problems they've encountered with the system they're using. In the past, pharmacy technicians had to manually inspect each medication in the kit to know what needed to be replaced or exchanged due to expiration. With RFID, each item is tagged with the NDC number, lot number, and expiration date. Anything missing can then be identified via an RFID scanner so you'll know what needs to be replaced. This helps to improve the efficiency of checking kits. An entire tray can be accounted for at once. Still, these systems are not perfect.

One problem occurs when a kit is opened and a medication is used and then returned to the kit, which is sent back to pharmacy. When pharmacy scans the used kit for missing items, the technology doesn't pick up on the fact that the opened vial is still in the kit, therefore the empty or partially used vial is not replaced. The failure to replace an empty vial can cause a delay in therapy. The hospital reported that this happened when rocuronium was not available in a kit as a case was ready to start.

Other hospitals have also reported problems. For example, an open vial of propofol returned with a used anesthesia kit was missed. Another hospital reported a situation where an RFID tag fell off the product and remained in the code cart tray after patient resuscitation. The drug was not replaced because the RFID system indicated that the drug was still there, since the drug tag was still there. Another issue is that scanning doesn't detect special arrangements of vials. As long as the right number of vials is present and they

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Limit access. Eliminate the storage of neuromuscular blockers in areas of the hospital where they are not needed.[7] 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 eliminate storage 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.[7] In areas where they are needed, place neuromuscular blockers in a lidded box or in a rapid sequence intubation (RSI) kit. One option is a highly visible red-orange storage 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. Also segregate neuromuscular blockers from all other medications in the pharmacy by placing them in separate lidded containers in the refrigerator or another secure, isolated storage area. Organize anesthesia carts and trays to avoid the proximity of look-alike vials, syringes, or bags, 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 also 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 is questionable because they make all vials look alike.

Dispense from pharmacy. 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 labeled, prefilled syringes and prepared infusions of neuromuscular blockers (and other anesthesia drugs) dispensed by pharmacy, commercially available, or outsourced, rather than self-prepared syringes or infusions.[9] Properly labeled, prefilled syringes have the potential to improve system safety, reduce syringe swaps, and enhance work efficiency.[10] Never dispense a neuromuscular blocker to a unit that cannot support mechanical ventilation.

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.[11,12]

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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have not expired, the system won't detect if these are placed in the wrong bin.

The bottom line with RFID technology is that it doesn't solve the human element of people leaving an RFID tagged—but used—vial in the kit. Basically, each vial in the kit still has to be visually inspected to ensure that it hasn't been used and just placed back into the kit. Of course, such problems are not unique to an RFID tag system. The same issues could occur with manual systems when a cursory review of code tray contents fails to detect an empty or partially filled vial. The RFID tag system is a step in the right direction, but not a complete solution to a tedious process.

Special Announcements

ISMP webinars

Join us on **June 27** for our next webinar, ***An Anesthesia Perspective: Tackling Medication Safety Challenges***. Our speaker will highlight medication-related challenges with anesthesia care, including the management of malignant hyperthermia, use of reversal agents, continuous monitoring during opioid infusions, safe labeling in the surgical setting, and much more.

Join us on **July 20** for our popular annual webinar, ***2016 Update on The Joint Commission Medication-Related Standards***. Frequent challenges associated with medication-related standards and National Patient Safety Goals will be presented along with examples of how to achieve compliance.

For details, visit: www.ismp.org/sc?id=349.

ISMP Medication Safety INTENSIVE

Are you going to be in Las Vegas in December for the American Society of Health-System Pharmacists Midyear Clinical Meeting? If so, join your colleagues at the ISMP **Medication Safety Intensive (MSI)** workshop. To see our ad in the *Hospital Pharmacy* journal, visit: www.ismp.org/sc?id=1747.

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Secondary Recommendations

Reduce the risk of IV admixture errors. Adopt IV workflow technology that utilizes barcode scanning of products during pharmacy IV admixture preparation. Systems that support barcode scanning and gravimetrics can assure proper drug selection and correlation to individual patient's orders. To be maximally effective, the system should be utilized for all compounded admixtures. Please refer to the ISMP **Guidelines for Safe Preparation of Sterile Compounds** (www.ismp.org/sc?id=461) for details (currently being updated).

Reduce the risk of batching errors. Compound one drug batch at a time, and verify and label the products before beginning any subsequent single or batch preparations.

Reduce unsafe mnemonics. Review order entry systems to identify problematic mnemonic auto-fill entries and label generation associated with neuromuscular blockers, and implement safer computer rules for mnemonics when indicated.[3]

Provide warnings on pharmacy labels. Ensure that pharmacy work labels and infusion/product labels for neuromuscular blockers are clear and accurate, and contain all necessary warnings.[3]

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, prepared and labeled 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.[7]

Flush the line. If a neuromuscular blocker has been administered, all of the drug should be flushed from the IV line or the line changed (and any source container removed) prior to extubation.

Timely dispensing and prompt removal. Pharmacy should practice just-in-time dispensing of neuromuscular products when possible to avoid unnecessary access to these products before use. When the drugs are no longer needed, place unused/partially used vials, bags, and syringes of neuromuscular blockers in a sequestered bin for return to the pharmacy. Unused patient-specific doses 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.[3] 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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