May 19, 2022 ■ Volume 27 Issue 10

ISMP
An ECRI Affiliate

# Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

## *Are you well positioned to resolve conflicts with the safety of an order?*

## Learning from a physician's homicide trial and the firing of multiple healthcare workers

A former Ohio physician accused of hastening the deaths of 14 patients by prescribing large doses of opioids for terminally ill patients was recently found "not guilty" of homicide.[1] The jury of 12 told the judge that they were at an "impasse" several days into the deliberation, but the judge instructed the jury to keep deliberating, and the jury reached a "not guilty" verdict 2 days later. While the opioids were administered to patients at the end of life after removal from a ventilator, the verdict was unexpected. Unusually large doses, such as 2,000 mcg of fenta**NYL** intravenously (IV), had been prescribed.[2] Sometimes the doses were repeated and administered along with a benzodiazepine and/or another opioid such as **HYDRO**morphone.[3]

Although the prescribing physician was acquitted of homicide, the State Medical Board of Ohio permanently revoked his medical license.[4] Additionally, the event led to the firing of more than 20 pharmacists and nurses at the hospital, the referral of dozens of practitioners to state professional boards for possible disciplinary action (e.g., reprimands, suspensions or permanent revocation of their licenses), and numerous civil lawsuits against the hospital and the health system.[5-7] Fortunately, the prosecutor's office stated that no nurse or pharmacist associated with this case would face criminal charges for their involvement in the patients' deaths.[1]

During testimony at the trial, it was clear that some practitioners who worked with this physician felt uncomfortable with the medication orders.[2] Still, for 4 years (2015-2018), the physician prescribed high opioid doses for numerous end-of-life patients, and various nurses administered these high doses after removing the medications from an automated dispensing cabinet (ADC), mostly via override before a pharmacist could verify the order. How did something like this occur and continue for 4 years? The following discussion explores that question and provides recommendations to help practitioners and health systems address concerns with the safety of an order when they arise. This includes the development of an established escalation process to promptly resolve these disputes.

### Intimidated by the Prescriber's Exceptional Reputation

Unfortunately, healthcare practitioners do not always bring their concerns about the safety of a medication order to the attention of the prescriber, particularly if the prescriber has an exceptional reputation.[8] During the homicide trial, three witnesses spoke about the physician's admirable reputation and how he had been a mentor to staff members, teaching them ways to improve patient care. One intensive care unit (ICU) nurse described him as, "Just a genuine guy when he was talking to family members and powers of attorney about how sick the patients were," adding that, "I believe he cared for his patients deeply."[9] Nurses also testified that they had not received formal training about fenta**NYL** or opioid dosing and, thus, felt the need to trust the physician's judgement.

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## NANALERT

### Potassium chloride for injection concentrate in EXCEL plastic bags

On May 17, 2022, ISMP, the American Society of Health-System Pharmacists (ASHP), and the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) issued a ***National Alert Network (NAN) Alert*** (www.ismp.org/node/31719) with recommendations to prevent an error with the new presentation of B. Braun's potassium chloride for injection concentrate (2 mEq/mL) pharmacy bulk package, which is now provided in a 250 mL EXCEL plastic bag (www.ismp.org/ext/901). The product was formerly available in glass containers, but the company's glass manufacturing line was decommissioned in the first quarter of 2022. This highly concentrated potassium chloride injection bag looks remarkably similar to intravenous (IV) infusion bags with blue and red labeling. A fatal error would almost certainly happen if this product was accidentally administered undiluted.

Organizations that use this product should review the *NAN Alert* and take immediate steps to prevent a potentially fatal medication error. This includes ensuring that only the pharmacy can purchase, store, and use this product; segregating this product away from other similar-looking infusion bags in pharmacy storage; affixing auxiliary labels on the case and both sides of the overwraps and bags; and scanning the barcode on the bag, as well as the barcodes on all IV infusion bags (to ensure none are potassium chloride for injection concentrate).

A dialogue between ISMP and B. Braun is underway about additional ways to enhance the proper identification of this product to reduce the risk of confusion.

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In our 2021 survey about disrespectful behaviors, 33% of more than 1,000 practitioners had assumed a medication order was safe in the past year because of the stellar reputation of the prescriber, despite their concerns about the safety of the order.[8] They assumed that the prescriber knew more than they did about an unfamiliar medication, or they feared falling out of favor with the prescriber if they questioned an order.[10]

## Convinced the Dose Was Safe

Did practitioners question the high opioid doses prescribed by the former physician? Yes, it appears that a few practitioners had contacted the physician to express their concerns. During the homicide trial, one ICU nurse noted that a pharmacist had reviewed and rejected an order for 1,000 mcg of IV fenta**NYL**.[9] Yet, the physician allegedly assured an ICU nurse on multiple occasions that "the order was good to go." According to a news report, when the physician was questioned by nurses and pharmacists regarding the high-dose orders, he would offer a long explanation to justify the order, touting his residency work as an anesthesiologist at a prestigious academic medical center.[2]

This is a less obvious but no less dangerous risk related to the culture that often goes unnoticed until a serious adverse event happens: staff speak up about potential safety concerns, but they are easily convinced that their concerns are unfounded. Surprisingly, many harmful prescribing errors that reach patients share this common factor: at least one person—a healthcare practitioner, patient, or family member—felt there was a problem with the order before the medication was dispensed and/or administered.[11] When practitioners, patients, or family members voice a concern, an explanation from a practitioner may dispel the initial concern too quickly before it has been given sufficient consideration. A pharmacist reassures a technician that the compounding directions are correct when questioned about an unusual volume of ingredients; a pharmacist assures the nurse that the strength of the infusion is correct when questioned about the final volume; a nurse reassures a patient that the medication is correct when questioned about its appearance; a physician convinces a pharmacist that the prescribed dose is correct when questioned because it differs from a protocol—these are all-too-frequent examples that have led to fatal adverse drug events.[11]

In our 2021 disrespectful behavior survey, nearly half (47%) of the respondents said they have felt pressured to accept an order, dispense a product, or administer a drug despite their concerns about its safety.[8] Practitioners reported that they sometimes move forward despite a feeling that something is wrong because they are unable to express their concerns clearly, or the concern is not taken seriously by the prescriber.

## Defining a Process

At your practice site, do staff always feel comfortable reaching out to a prescriber to address concerns when a prescribed treatment varies from the expected standard of care, or when duplicate therapy is prescribed, or when a medication dose exceeds what is typically considered safe? Are you confident that the prescriber takes all expressed concerns about the safety of an order seriously? Furthermore, if a conflict in the safety of an order arises in which the prescriber does not take the expressed concern seriously, does your organization have a clear and well-known escalation process to promptly resolve the dispute? Although the process for handling drug therapy concerns objectively and professionally may vary to meet the unique needs of individual organizations, consider the guidelines below when developing or revising your process.

## Conflict Resolution Guidelines

**Gather information.** If a nurse, pharmacist, or other healthcare professional suspects that an order is potentially incorrect based on either toxicity (e.g., overdose) or efficacy (e.g., wrong antibiotic), they should gather information to present to the prescriber when contacting them about their concern. A nurse may contact a pharmacist to help research the issue so factual information that supports the expressed concerns can be

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## SAFETY briefs

**ISMP relieved by Vaught sentence.** ISMP is relieved that RaDonda Vaught did not receive a prison sentence after her conviction for impaired adult abuse and criminally negligent homicide stemming from a fatal medication error. The judge sentenced her to 3 years of supervised probation on a diverted sentence, after which her record could be wiped clean. While RaDonda will likely never work as a registered nurse again since her license in Tennessee was permanently revoked, we commend the judge for using the power of the law with integrity and humanity during the sentencing. As we continue to grieve the loss of Charlene Murphey, we call on all healthcare providers to consider if similar risks exist where you work, and to meet internally to plan immediate proactive interventions.

**Safe practices during contrast media shortages.** Many organizations have been impacted by the expanding shortage of iodinated contrast media. Conservation strategies include order review to assess the appropriateness of alternative contrast agents, and when appropriate, delaying scans that are not clinically urgent, or switching to a computed tomography (CT) scan without contrast or to a non-CT modality (magnetic resonance imaging [MRI] or ultrasound). Our affiliate, ECRI, has posted on its COVID-19 Resource Center, a complimentary report that provides information about marketed contrast media and its availability (www.ismp.org/ext/912). The report can be used to consider equivalent products while navigating contrast media shortages. The American Society of Health-System Pharmacists (ASHP) has created an additional resource with considerations for imaging contrast shortage management and conservation (www.ismp.org/ext/913).

We have heard that some organizations have attempted to maximize the use of a single dose vial of contrast media. However, organizations should be aware of the risks of inappropriate use. Single dose vials are meant for use in a ***single patient for a single case, procedure, or injection***. Medications in these vials typically lack antimicrobial preservatives and can become contaminated when used

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clearly communicated to the prescriber. The pharmacist or nurse might need to review the patient's health record; talk with the patient; use reputable drug information resources; and consult other nurses, pharmacists, or physicians to gather the information needed to communicate the drug order concern effectively.

**Question the order.** Organizations should foster a culture of safety that enables pharmacists and nurses to not fear questioning an order when they have reason to believe a patient is at risk, or even if they just have a sense that something is wrong. To help overcome fear, practitioners can focus on which would be worse: to be wrong, or to allow an injury to a patient. Any questionable order should be discussed directly with the prescriber. The use of a standard communication strategy, such as SBAR (www.ismp.org/ext/902) or TeamSTEPPS (www.ismp.org/ext/903), can help frame the discussion.

If applicable, the pharmacist or nurse should ask the prescriber for documentation (e.g., protocols, journal articles) supporting the order and read any materials provided. Statements such as "the protocol says to do it this way" or "that's how they do it at another hospital" should never be accepted as proof and should signal the need for further investigation.[11] Check with risk management regarding the best way to document any safety concern and the prescriber's response to the concern.

If the prescriber will not change the order and the practitioner is still not satisfied that the patient will not be harmed, the prescriber should not be asked, nor allowed, to personally administer the drug. Transferring responsibility to the prescriber for possible patient harm is not likely to absolve the questioning practitioner if patient harm occurs. Instead, escalate the concern on behalf of the patient.

**Escalate the concern.** A healthcare practitioner's persistence in communicating recognized, or even vague, concerns about the safety of an order can clearly prevent harmful errors from reaching patients, even when the perceived problem is met with opposition from experts. Thus, an effective process for handling medication therapy conflicts requires more than a hierarchical structure of referring problems up the chain of command. Staff members also need clear guidance and support from organizational leaders to follow when those in authority, such as a prescriber, do not agree with their expressed concerns. Unfortunately, more than half (58%) of respondents to our 2021 disrespectful behavior survey said their organization's process for handling clinical disagreements does NOT allow them to bypass a typical chain of command if necessary.[8] Thirty-seven percent of respondents could not answer the survey question on this topic because they did not know if they could bypass the chain of command.

In cases involving conflict between a prescriber and a healthcare practitioner who clinically cannot determine how to proceed, there must be a formal process that allows clinical staff to bypass the chain of command up until the point where everyone feels that it is clinically appropriate to move forward. For example, the prescriber's chief resident, attending physician, department chair, or a specialist in the area of the ordered drug therapy might be contacted. Escalation outside of a particular department may be needed, which might include contacting a hospital administrator or a defined senior leader to mediate the difference of opinion. Or an escalation team identified by senior leaders might be rapidly deployed for handling conflicting opinions objectively and professionally, beyond the walls of the patient room. Depending on the nature of the patient care disagreement, the escalation team could include the department chair or a practitioner with expertise in a subspecialty. The goal is to deploy a clinician or a team with knowledge about the issue, the skill to mediate, and the power to resolve the issue outside of the usual chain of command. Resolution of the issue needs to be accomplished in a timely fashion to ensure that the patient is cared for in the moment.

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inappropriately, serving as a source of infection. In 2012, we cited a Centers for Disease Control and Prevention (CDC) *Morbidity and Mortality Weekly Report* (MMWR) about bacterial infections following the use of a single container of contrast media for multiple patients (www.ismp.org/node/659). According to the CDC (www.ismp.org/ext/914), in times of critical need, the contents of unopened single dose vials should ONLY be repackaged for multiple patients under ISO Class 5 conditions by qualified personnel in compliance with USP <797> *Pharmaceutical Compounding-Sterile Preparations*. Thus, in radiology, transferring the contents of single dose vials to syringes for more than one patient is NOT safe. Manufacturers' recommendations must also be followed pertaining to safe storage of the medication outside of its original container. Since repackaging from single dose vials deviates from medication and regulatory guidance, ensure institution approval prior to pharmacy repackaging of contrast media.

Pharmacists should attend staff meetings periodically in units where contrast media is used to discuss its safe use, especially during this shortage. We understand some organizations that provide contrast media do not have an on-site pharmacy with a sterile compounding area. These sites should consult with infection prevention and pharmacy professionals, including those who work at compounding pharmacies with ISO Class 5 conditions.

**Companies begin move toward full implementation of ENFit.** As organizations move toward full implementation of ENFit, manufacturers will begin to phase out legacy feeding tubes, syringes, and bags with attached administration sets for enteral feedings. Currently, enteral administration sets have an ENFit connector, but they also have a transition adaptor to connect with legacy feeding tubes. However, Cardinal Health (in July 2022) and Moog Medical (later this quarter) will begin removing the transition connectors from their administration set assemblies. Transition connectors will still be available, but only as stand-alone items. Furthermore, Cardinal has announced that, in July 2022, adult and pediatric nasogastric feeding

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If the patient's well-being is likely to be compromised while escalating the concern, and the patient's clinical condition requires immediate attention, we have previously recommended calling a rapid response team.[10] Rapid response teams are triggered by patient deterioration or a change in clinical status and are designed to respond accordingly to facilitate stabilization. However, a rapid response team should not be called to resolve treatment conflicts between healthcare practitioners, as the team likely will not include experts in the topic under question. If needed, a rapid response team should focus on patient care, and an escalation team should focus on resolving the conflict in a timely fashion.

## Conclusion

We strongly encourage organizations to review this case at their medication safety committee meeting and to develop a process that swiftly and appropriately responds to conflicts about the safety or efficacy of an order. To promote the need to speak up and to persist with any concerns about the safety of an order, the conflict resolution process should be included in employee orientation and practiced in simulations to increase awareness and improve comfort levels.

The hospital where this event happened has established a new escalation policy for orders that are concerning or represent deviations in established protocols. The hospital also limited the amount of specific medications available for emergency override through an ADC, set maximum dosages for pain medications in the electronic health record, increased education on end-of-life care, and now more closely monitors the appropriateness of ADC overrides.[2] If your hospital has not already done so, consider taking these steps, as well.

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# Patients swallowed the desiccants in everolimus blister cards

**PROBLEM:** We have received reports about patients swallowing desiccant tablets that are packaged within blister cards holding everolimus tablets from Biocon Pharma. Everolimus is used primarily to treat certain forms of breast or renal cancer, noncancerous fat and muscle tumors in the kidney (renal angiomyolipoma), and to prevent rejection after liver or renal transplantation. The medication is available in 2.5 mg, 5 mg, 7.5 mg, or 10 mg tablets. Each strength is packaged as a carton of four blister cards, and each blister card has seven blisters containing everolimus tablets and four blisters containing desiccant tablets. The desiccant blisters are labeled with "DESICCANT DO NOT EAT" (**Figure 1**, page 5), but this warning is only printed on one side of the blister card; the other side contains no wording (**Figure 1**, page 5). Patients viewing the blank side of the blister may push a desiccant tablet through without realizing it. Although the desiccant tablets

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tubes, pediatric extension sets, and gastrostomy feeding tubes will **only** be manufactured with the ENFit design. The Global Enteral Device Supplier Association (GEDSA) posts manufacturer updates on its website (https://stayconnected.org) and has compiled the most recent information in a PDF document, which can be found at: www.ismp.org/ext/911.

**Atropine prefilled syringes with sealed syringe tips.** We recently received a report about atropine prefilled glass syringes (1 mg/10 mL) with sealed syringe tips that will not allow injection. The syringes are manufactured by Intas Pharmaceuticals for Accord Healthcare (NDC 16729-484-03). A hospital reported nine such syringes across multiple lot numbers (not all recorded but including lots M2107942 and M2107940). The reporting facility noticed that the affected syringes usually had a small but visible

**Figure 1.** Rather than having an opening at the tip, the syringe is completely sealed with what appears to be a "bubble" of glass (arrow), and the user is unable to expel atropine (Intas Pharmaceuticals) from the syringe.

"bubble" of glass (**Figure 1**) at the syringe tip. This was discovered by nurses who attempted to administer atropine but were unable to expel the medication, which caused delays in administration during medical emergencies.

We have reported this issue to the manufacturer and to the US Food and Drug Administration (FDA). For now, we encourage you to proactively inspect your inventory for this defective product. If you discover this atropine syringe is in stock, we recommend removing it from inventory and purchasing prefilled syringes of atropine from an alternative manufacturer.

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look different than the everolimus tablets, these can still be easily mistaken for medication-containing tablets. Thus, patients have accidentally ingested a desiccant tablet instead of an everolimus tablet.

Since February 1, 2021, the ***ISMP National Medication Errors Reporting Program*** (ISMP MERP) and the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) have received 13 reports related to this issue. Although at least eight manufacturers provide everolimus tablets in blister packaging, all of the reports submitted to FDA and ISMP involve the product from Biocon Pharma, which is the only company that packages desiccants with the tablets in blister cards. The cases frequently involved elderly patients for whom poor vision may have contributed to the confusion. Furthermore, the font size and light tan color of the drug name and dose on the labeled side of the card are difficult to see on the foil blisters (**Figure 1**).

Two patients almost ingested the desiccant. In one case, a non-English speaking patient became confused about the desiccant blisters and thought he was supposed to swallow them along with the medication. Luckily, he called the pharmacy, and the pharmacist was able to communicate with the patient to avert an error. The other 11 patients ingested the desiccant, often for several doses. In two cases, parents administered the desiccants to their children. One mother questioned whether her child's recent erythematous face was related to ingesting the desiccant after discovering she had administered the desiccant to her child at least six times. Another patient took all four desiccants in the blister pack and went to the emergency department for chest pain. We should also mention that the everolimus product labeling and the information that accompanies the medication dispensed to patients provide NO information about the desiccants and what to do if they are swallowed.

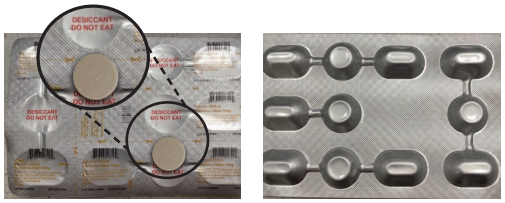


**Figure 1.** Front and back of everolimus 10 mg blister card, which holds seven medication tablets (oblong) and four desiccants (round). The desiccant removed from the blister looks like an oral tablet. The blister card is labeled on the front (left), but not on the back (right).

Biocon Pharma told us that the desiccants in everolimus blisters are chemically inert, non-toxic, and non-hazardous. They are a moisture absorbing mixture of molecular sieve, resin-polypropylene, white colorant, and a trade secret binder. According to the manufacturer, the desiccant tablets are not absorbed or digested, passing through the body as is. Still, keep in mind that patients swallowing a desiccant tablet may also miss a dose of their scheduled cancer or immunosuppressant medication, which could impact their treatment.

We have previously published reports about patients who have accidentally ingested desiccant cylinders found in some manufacturers' oral medication bottles. For example, an elderly patient with poor eyesight nearly asphyxiated when he gagged on a desiccant cylinder in his medication bottle. A literature search confirms these cases, some of which required surgical removal of the desiccant due to esophageal obstruction (www.ismp.org/ext/897; www.ismp.org/ext/898).

**Safe Practice Recommendations:** Many practitioners will never open the Biocon Pharma everolimus carton to see the individual blister cards, so it is important to alert them to the blister card labeling issue so they are aware of the potential for patients to ingest the desiccant tablets. When educating patients upon discharge, it is critical to let them know that these blister cards contain desiccants that might be mistaken as tablets. Patients should be warned to never swallow or eat a desiccant. Additionally, please remove desiccant cylinders from medication bottles when possible; if the desiccant must remain in the bottle, warn patients about the hazards associated with swallowing it. We have reached out to Biocon Pharma and FDA to notify them of the concern with everolimus labeling so they can take steps to properly address the above issues.

## Special Announcements

### Public comment on draft guidelines

Draft guidelines to promote safe medication practices in perioperative and procedural settings have been posted for public comment through **May 27, 2022** (www.ismp.org/node/31601). The guidelines address key medication risks in the perioperative setting.

### FREE webinars for pharmacy technicians

Join us as we present two **FREE** webinars, supported by Baxter, on the role that pharmacy technicians play in sterile compounding safety. Register at the links provided.

- **May 25, 2022:** ***Ensuring Sterile Compounding Safety: A Leading Role for Pharmacy Technicians*** (www.ismp.org/node/31393)
- **June 7, 2022:** ***Sterile Compounding Technology: Pharmacy Technicians Lead the Adoption of Best Practices*** (www.ismp.org/node/31395)

### FREE webinar recording

On May 6, 2022, leaders from ISMP and The Just Culture Company presented a **FREE** webinar, ***Lessons Learned about Human Fallibility, System Design, and Justice in the Aftermath of a Fatal Medication Error***. An overview of a fatal medication error was presented. The panel then discussed common system vulnerabilities and key strategies to help prevent a similar tragedy, as well as providing a risk model of the error and how it might be viewed within a Just Culture. To listen to (and view) the webinar, visit: www.ismp.org/node/31106.



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