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ISMP
An ECRI Affiliate

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

Safety considerations during expedited product approval

Problem: Many organizations have developed a process for formulary additions as described in the ***American Society of Health-System Pharmacists (ASHP) Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System*** (www.ismp.org/ext/1096). Often, a prescriber's request for a new medication initiates the process. The prescriber may fill out a form and provide supporting data, including applicable studies, to justify its addition to the formulary. A designated pharmacist (e.g., drug information pharmacist, clinical manager, director of pharmacy) reviews the request and assesses the availability, clinical appropriateness, safety, cost, and utility of the medication. The information is compiled for discussion at a pharmacy and therapeutics (P & T) committee meeting, where the requesting prescriber may be invited to present their recommendation. If approved by the committee, the formulary request then goes to the medical executive committee, where the medication is officially approved (or denied) for addition to the formulary. The medication typically will not be available for use until it is added to all medication-use systems (i.e., electronic health record, order entry systems, drug libraries).

The above process often takes a few months. However, there are times when a prescriber may request a non-formulary medication urgently or when an important formulary medication is unexpectedly not available, such as during a shortage. Because of this serious need, the new medication or formulation may be added to the medication-use system quickly, without going through the formal formulary approval process.

Challenges. Not having a medication on formulary can cause delays in treatment, resulting in preventable adverse drug events. However, without a comprehensive process to evaluate any safety concerns, organizations might purchase less than desirable products and miss critical steps when introducing a new product (e.g., staff education, inspection of the label). Consider the following events.

*An organization reported cases of morphine overdose during a morphine sulfate oral solution shortage. Historically, the organization purchased morphine 5 mg/5 mL unit dose cups, but since the cups were not available, the pharmacy purchased morphine 10 mg/5 mL by Precision Dose (NDC 68094-001-59) (**Figure 1**). The product label states, "10 mg/5 mL" and "Delivers 5 mL," but nurses mistook this as delivers **5 mg** and administered more than the intended dose to several patients before the error was discovered.*

Figure 1. Label of a 10 mg/5 mL unit dose cup of morphine sulfate by Precision Dose that replaced a 5 mg/5 mL unit dose cup during a shortage.

After a respiratory therapist reported that sterile water for inhalation bottles connected to a humidifier device were leaking, the organization's materials management department purchased 1,000 mL sterile water for inhalation bags instead of bottles. Fortunately, when rounding on a patient care unit, a pharmacist discovered the bags and expressed concerns that the 1,000 mL sterile water for inhalation bags may be confused with other 1,000 mL bags and could be accidentally administered intravenously

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Death from air embolism after pneumatic tubing was connected to IV line. The US Food and Drug Administration (FDA) recently added a case to their "Examples of Medical Device Misconnections" webpage, about an event in which a pneumatic (air inflation under pressure) tubing line from a noninvasive vascular diagnostic system was erroneously connected to an intravenous (IV) catheter (www.ismp.org/ext/1109). The case was reported to the FDA earlier this year.

An ultrasound exam is a noninvasive vascular diagnostic system that may involve obtaining a blood pressure measurement to assess the arterial blood pressure differences between a patient's arms and legs. However, a vital sign monitor with attached pneumatic tubing to inflate a blood pressure cuff could also be misconnected. As in the case shared by FDA, the pneumatic tubing used to inflate the cuff during the procedure had a Luer connector that was compatible with the patient's IV catheter (**Figure 1**, page 2). The connector was erroneously attached to the patient's IV catheter. As a result, air was injected into the IV line and the patient died from an air embolism.

This latest case is similar to others we have written about over the past 20 years. For example, in one article, we wrote about tubing from a portable blood pressure monitoring device being inadvertently connected to the patient's IV line, risking, or even causing a fatal air embolism (www.ismp.org/node/65502). In our September 4, 2003, acute care newsletter, we wrote about the inadvertent connection of an air supply hose from a sequential compression device (SCD), also referred to as an intermittent pneumatic compression (IPC) device, to a needleless IV tubing port. In that case, the SCD was turned off and the misconnection was found before any patient harm occurred.

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*(IV) to patients. The pharmacist recommended that when large volume bags of sterile water must be used outside of the pharmacy, the best approach is to use containers that look different than 1,000 mL bags of IV solutions, such as 2 liter bags, or bottles of sterile water, to prevent the inadvertent administration of sterile water via the IV route (**Targeted Medication Safety Best Practices for Hospitals**, Best Practice #10 [archived], www.ismp.org/node/160). Without pharmacy oversight, there is an increased risk of medication errors when medications and related products are purchased by other departments.*

Safe Practice Recommendations: Organizations should have a well-defined process for formulary additions and new medication-related products or devices. The process must account for urgent needs and provide step-by-step guidance. Consider the following recommendations to support an expedited process.

Conduct a safety analysis and act. While it might not be feasible for organizations to complete a full failure mode and effects analysis (FMEA) to evaluate all of the risks when a new product needs to be brought in, organizations must have plans in place to evaluate safety concerns to avoid medication errors. Call it a safety analysis or risk analysis, the idea is to proactively consider product characteristics that might cause confusion and lead to medication errors, then develop strategies to prevent those errors. The process should include concerns about errors that might happen during product procurement, drug storage in the pharmacy and clinical areas, prescribing, product selection, preparation, dispensing, distribution, and administration. In addition, technologies used for ordering, compounding and distribution, drug storage, and administration should also be assessed. This analysis should enable appropriate actions when needed to prevent serious failures or, if the risk is too great, a decision not to use the product at all. This process and the necessary steps/questions should be defined for expedited formulary addition processes.

A sample format for a "mini FMEA," which was shared by OhioHealth Pharmacy Services, is available in **Table 1**, page 3. These types of standardized questions should be used as a template to address aspects of the medication-use process while conducting a mini FMEA to uncover potential hurdles and/or barriers within your organization.

Involve key personnel. Outside the standard formulary approval process, establish an expedited method for an urgent need managed by designated pharmacy leads. Depending on your organization, this may include the director of pharmacy, medication safety officer, operations manager, clinical manager, drug information pharmacist, buyer, and/or informatics pharmacist. Identify subject matter experts who need to be involved early on in the process to help expedite post-approval implementation.

Also, gather feedback from frontline staff to generate a comprehensive list of potential issues to address. Depending on the medication or related process change, the pharmacy should consult with appropriate individuals in other impacted areas (e.g., nursing, anesthesia, medical department chair, respiratory therapy, infectious disease, laboratory services) or notify them of the upcoming change. Those responsible for pharmacy operations should be included in the process as soon as possible to ensure appropriate resources are available and identify potential hurdles that must be considered when implementing a change (e.g., appropriate storage space for the addition of a high-volume product in refrigerators or stockrooms, staffing requirements to accommodate increased drug compounding).

These designated pharmacy leads may want to consider convening regularly to proactively monitor known shortages and evaluate stock levels and current/historic usage to avoid urgent situations whenever possible. Consider early action steps like therapeutic substitutions, formulary use restrictions, or IV to oral conversions when feasible to help conserve supplies until more are available.

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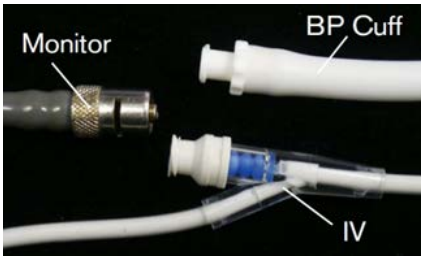

Figure 1. In our June 12, 2003 issue, ISMP showed how blood pressure monitor tubing could connect easily to either the blood pressure (BP) cuff tubing or the Y-site of IV tubing that was being used at the time (changes to the connectors may have been made since then). Note how similar in appearance the IV tubing (with propofol) is to the blood pressure cuff line.

The best solution is to eliminate interconnectivity between various medical tubing connections. Currently, there is an International Organization for Standardization (ISO) standard 80369 that addresses connectors that allow the pneumatic flow of gases via a limb cuff connection (e.g., SCDs, pneumatic tubes to blood pressure cuffs). This ISO standard is the same standard that addresses misconnections with enteral (ENFit), neuraxial (NRFit), and vascular connectors (Luer). The recognized standards have been evaluated by the FDA, and manufacturers are encouraged to apply these standards to medical devices, as appropriate.

While connections between pneumatic and vascular systems may be rare, no doubt some misconnections are corrected before serious injury occurs and not all incidents (close calls) get reported to the FDA. According to the FDA, misconnections can happen with devices that have not incorporated connector designs conforming to the new standards. Therefore, the FDA encourages providers to report incidents even if the misconnection was corrected before reaching the patient. In addition, the FDA says they will continue to work with manufacturers, standards organizations, federal partners, professional societies, advocacy groups, patients, and other stakeholders to reduce the chance of medical device misconnections and patient harm. Perhaps they could help move this along by developing guidance for industry that more formally requires the use of the ISO standard when medical devices are being manufactured.

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Table 1. Mini failure mode and effects analysis (FMEA) for new/alternative drugs*

Potential Risk Factor	Yes	No	Method(s) of Safety & Comments
Have specific errors with this product been reported in the literature (e.g., The Joint Commission Sentinel Event Alerts, ISMP newsletters)?			
Is the product a high-alert medication or hazardous medication?			
Does the product have an approved Risk Evaluation and Mitigation Strategy (REMS)?			
Is this product a biosimilar or interchangeable biological product?			
Does the product labeling clearly express product characteristics necessary for safe use?			
Are there other products with names that look or sound like this product?			
Is there a high risk of a calculation error during prescribing, dispensing, or administration?			
Does the product contain latex?			
Are there policies and procedures that need to be rewritten or amended before the product is approved for formulary use (e.g., policy, guideline, ordering restrictions, and/or order set)?			
Will this medication be used in any special patient populations (e.g., pediatrics, geriatrics) that require additional precautions to prevent medication errors?			
Does this product require that specific alerts (or changes in existing protocols) be configured in the electronic health record or smart pump drug library?			
Will this be dispensed in a ready-to-administer form?			
Are there multiple steps to product preparation?			
Are there any handling precautions with this product?			
Can this medication be delivered safely by the pneumatic tube system?			
Should this medication be available on any automated dispensing cabinet (ADC) override lists?			
Does the product require administration over a given amount of time (rate) that, if not adhered to, may cause harm?			
Does this product need to be administered in specific clinical locations in which staff need to acquire specific skill(s) to be able to administer this product?			
Does the administration of this product require an independent double check during preparation or administration? (If so, what are the components of the double check?)			
Is it likely this product could be inadvertently administered by an alternative route (e.g., oral liquid administered IV)?			
Is this drug a vesicant or an irritant?			
Does this product require specialty monitoring (e.g., cardiac monitor, pulse oximetry, capnography)?			
Is there a parameter (e.g., laboratory value, vital sign) that needs to be monitored to ensure efficacy or to minimize the risk of toxicity?			
Is there an effective treatment if the patient experiences undesirable side effects or an overdose?			
Is the antidote or rescue treatment readily available in the location where the product is administered?			
Are emergency instructions for use readily available to staff?			

***Source:** Modified with permission from OhioHealth Pharmacy Services

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Meanwhile, to protect patients, this is an issue that demands attention. Take the time to work with biomedical engineering to seek out medical equipment that will not connect to vascular systems. When possible, place blood pressure cuffs on a different limb than an IV site and remove IV catheters as soon as they are no longer needed. Appropriately labeled IV lines could help alert staff if they are about to access that line accidentally. Educate staff, including nonclinical staff who work in patient care areas, about this hazard. Before any tubing is connected or reconnected to a patient, verify the access point, and trace the line toward the insertion site/cuff. While trained licensed practitioners can inadvertently connect the wrong type of tubing to an IV line, especially in a rushed environment or when their view is obstructed, recognize that unlicensed, untrained staff may disconnect or reconnect various tubing, or be inappropriately asked to perform specific tasks such as turning off pumps before patient transport. During orientation, and when possible, educate unlicensed staff about these risks and to deny requests to connect or disconnect any medical tubing.

HIGH-ALERT

Fewer high-alert drugs prescribed by dentists. ISMP has warned of the risk of respiratory depression associated with most sedatives used by dentists for pediatric sedation. In fact, we have written about dozens of error reports related to chloral hydrate and other drug-related oversedation in pediatric patients, some resulting in death.

In a recent study by Kim et al (Kim KC, Khouja T, Burgette JM, et al. Trends in dispensed prescriptions for opioids, sedatives, benzodiazepines, gabapentin, and stimulants to children by general dentists, 2012-2019. *Pharmacoepidemiol Drug Saf.* 2022;1-10. doi: 10.1002/pds.5589), we were pleased to see that prescriptions for opioids, benzodiazepines, sedatives, and other high-alert drugs prescribed by dentists for pediatric use declined by 63% from 2012 to 2019. However, the authors noted that in some low-income regions, there were still high rates of these medications being prescribed for dental procedures for older teens and children, and recommend additional research in these populations.

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Define the process. Develop a policy that outlines the potential risk factors and questions that must be addressed such as those mentioned in **Table 1**, page 3. To organize this information, some organizations may want to consider project management software or leverage technology that they currently have available (e.g., Microsoft Teams, Excel) to document methods of safety, assign responsibilities, and identify appropriate timeframes for each step.

Ensure a pharmacist approves medication-related products/devices. No drug-related item (e.g., fluids, syringes, prefilled flush syringes, medicine cups) should be purchased without pharmacy involvement/approval.

Include a post-implementation review. Monitor clinical and operational outcomes to evaluate how effective your process is. After a formulary addition or change, encourage staff to escalate any issues that arise to pharmacy administration. Use event reporting systems and data from technologies (e.g., smart pump data, barcode scanning data) to identify additional gaps in the process. Use this information to address steps that may have been missed, modify the potential risk factor/question template, and further refine the safety analysis process.

Evaluate non-formulary orders. Complete a comprehensive review of non-formulary medication orders regularly (e.g., quarterly) and use this data to assess which medications should be considered for formulary addition. Also, review utilization, or lack thereof, to analyze which medications can be considered for formulary removal.

Worth repeating...

SUMAtriptan injection – it's subcutaneous only!

SUMAtriptan injection for migraine and cluster headaches is to be administered only as a subcutaneous injection. In a recent case, a prescriber ordered subcutaneous **SUMA**triptan to treat a patient's migraine. A nurse drew up the dose but inadvertently administered it intravenously (IV). The patient experienced flushing without further complications. ISMP previously published (ISMP. Preventing **SUMA**triptan injection wrong route errors. *ISMP Medication Safety Alert! Acute Care*. 2018;23[11]:1-2) about similar events. Most errors have occurred while practitioners were administering several IV medications to patients, but didn't notice or forgot that **SUMA**triptan should only be administered subcutaneously. The organization that reported this most recent event has implemented a required field in the electronic health record (EHR) that prompts nurses to document the location of the subcutaneous injection prior to administration.

Figure 1. SUMAtriptan kit contains materials for subcutaneous injection, including a subcutaneous needle.

If pharmacy does not prepare and dispense syringes of **SUMA**triptan as needed, create a kit that contains the drug vial with an appropriate size syringe and subcutaneous needle (**Figure 1**). Add an auxiliary label to the kit to specify for "subcutaneous use only."

Another option is to stock the nasal formulation of **SUMA**triptan, which has a similar onset of action. There are also autoinjectors and pens available, but these are meant for self-injection by patients. To prevent these types of errors from occurring, manufacturers should provide subcutaneous medications in prefilled syringes with attached needles and safety guards to facilitate the correct route of administration.

Special *Announcements*

Virtual MSI workshops

Don't miss the opportunity to register for one of our unique 2-day, virtual ***ISMP Medication Safety Intensive (MSI)*** workshops. Learn how to identify risks before they cause harm and how to use data for continuous improvement. These programs fill up quickly, so register early. The virtual program dates for 2023 are as follows:

- **April 13-14, 2023**
- **June 8-9, 2023**
- **August 3-4, 2023**
- **October 4-5, 2023** (later start time for West Coast participants)

For more details about the program, please visit: www.ismp.org/node/127.

ECRI/ISMP patient safety webinar

Join us on **April 12, 2023**, for our webinar on the ***Top 10 Patient Safety Concerns 2023***. Speakers will discuss the recently released annual report that identifies the top patient safety challenges across the continuum of care. These challenges were identified through data analysis, the literature, and actual events reported to or investigated by our team of experts. Listen in to see how these concerns can help identify safety improvement opportunities within your organization. For more information and to register, visit: www.ismp.org/ext/1137.

NEW

ISMP **Targeted Medication Safety Best Practices for Community Pharmacy**

ISMP has developed the first set of specific, consensus-based guidance to help prevent persistent medication safety issues in community pharmacy and the potential patient harm that can result. ISMP hopes to inspire and mobilize practitioners to adopt the 2023-2024 ISMP ***Targeted Medication Safety Best Practices for Community Pharmacy***, some of which are applicable to other healthcare settings such as ambulatory, mail order, specialty pharmacy, long-term care, and home infusion.

Also Available:

A worksheet has been developed to assist in analyzing the current implementation status of the new community pharmacy *Best Practices*. To utilize this helpful tool, visit: ismp.org/node/67951

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To access the guidelines, visit:
ismp.org/node/65345