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

MERP annual review exposes how manufacturer labeling/quality issues impact medication safety

From July 1, 2023, through June 30, 2024, a total of 1,016 voluntarily submitted reports were sent to the ***ISMP National Medication Errors Reporting Program*** (ISMP MERP). Healthcare practitioners utilize ISMP MERP to inform others about medication safety issues they have experienced and to seek recommendations for needed improvements in product and practice safety. ISMP professional staff reviews every report submitted and utilizes them for their educational value. As necessary, regulators, standards organizations, and manufacturers are contacted, and reports are also considered for publication in the *ISMP Medication Safety Alert!* ISMP also operates a separate reporting program for vaccine-related issues and another for consumers to report events.

Almost half of the reports (47%) involved errors that reached patients. The remaining reports were classified as close calls (18%) (errors that happened but did not reach the patient) or hazardous conditions that warrant concern (35%). While the event location was not included in the majority of reports, 19% of reports were submitted by practitioners who work in inpatient settings and 12% from community pharmacies. Reports were also submitted from other settings (e.g., specialty pharmacies, physician offices, mail order pharmacies), but each of these represented 2% or less of the submitted reports. Errors occurred during all phases of the medication-use process but close to three-quarters happened during dispensing (37%), administration (21%), prescribing (8%), or procurement (8%). While the literature suggests administration and prescribing errors are most common, the high reporting of dispensing errors reflects the most common reporter type—pharmacy personnel. The medications most commonly involved included opioids (4.2%), antineoplastic agents (3.8%), insulin (3.4%), heparin (3.1%), antipsychotics (2.4%), and glucagon-like peptide-1 (GLP-1) agonists (2.2%). Reports were analyzed to identify potential contributing factors. The two most commonly reported factors were related to similar labels/packaging (16.6%) and manufacturer/labeler issues (13.3%).

Similar Labels/Packaging

Given that this issue continues to be a common theme in many of our newsletter articles, errors caused by look-alike packages and labels being the most common contributing factor is not surprising. For example, errors have been reported that involved mix-ups with **MYXREDLIN** (insulin human) 100 units/100 mL infusion bags and two other intravenous (IV) medication bags, **ZOSYN** (piperacillin and tazobactam) 4.5 g/100 mL (**Figure 1**) and **CARDENE IV** (ni**CAR**dipine) 40 mg/200 mL (**Figure 2**, page 2). All three products are manufactured by Baxter and have nearly identical packaging. In one case, the pharmacy dispensed a Myxredlin bag instead of the ordered Zosyn after the pharmacy technician inadvertently placed the Zosyn label on the Myxredlin bag. The nurse scanned the pharmacy-

Figure 1. Similar-looking Zosyn (left) and Myxredlin (right) infusion bags.

continued on page 2 — Manufacturer labeling/quality issues >

SAFETY briefs

Entire insulin infusion administered at fluid rate. A prescriber ordered a 100 unit/100 mL **MYXREDLIN** (insulin) infusion for a patient with diabetic ketoacidosis (DKA). The prescriber also ordered a 0.9% sodium chloride infusion for the patient at a rate of 500 mL/hour as part of the DKA protocol. The nurse labeled both intravenous (IV) lines and programmed each infusion using the smart pump drug library. A second nurse checked the pump programming and labeled lines and the infusions were initiated. Neither nurse traced the lines from the medication/infusion bags, through the pump channels, to the patient or vice versa. Shortly after, the pump alarmed to signal that the sodium chloride infusion was completed. The nurse returned to the patient's room and found that the insulin infusion had been placed in the pump channel for sodium chloride and the sodium chloride had been placed in the channel intended for the insulin infusion. The patient received 100 units of insulin in less than an hour. The nurse notified the prescriber and monitored the patient's blood glucose, which was less than 70 mg/dL. The prescriber ordered a dextrose bolus and infusion, and transferred the patient to the intensive care unit (ICU) for monitoring. Fortunately, glucose levels soon returned to normal, and the patient was transferred from ICU to an inpatient unit within 24 hours.

When infusions are started, reconnected, or changed (i.e., new bag/bottle/syringe), trace the tubing by hand from the solution container through the pump channel, and then to the entry site on the patient (or vice versa) to ensure the proper infusion is set at the intended rate (pump/channel) and is being administered via the correct route. Confirm the infusion dose and rate are programmed accurately in the pump and verify that the order in the medication administration record (MAR) and the medication label match what is programmed in the pump when performing line tracing

continued on page 2 — SAFETY briefs >

> Manufacturer labeling/quality issues — continued from page 1

generated barcode on the Zosyn label, rather than the manufacturer barcode on the bag and administered the insulin infusion. The patient was found unresponsive, a hypoglycemic protocol was initiated, and they recovered. In another case, a nurse replaced an empty Cardene infusion bag with a bag obtained from the automated dispensing cabinet (ADC) and administered it without using barcode scanning. An hour later, she returned to the patient's room, scanned the barcode on the infusing medication to document administration, and identified that the patient received approximately 40 mL of Myxredlin. During the ADC stocking process, a pharmacy technician had scanned the barcode on only one of the Cardene cartons (following the pharmacy's process) and placed a similar-looking Myxredlin carton in the Cardene bin in error.

Figure 2. Similar-looking Cardene IV (left) and Myxredlin (right) infusion bags.

Highly stylized graphics and prominent corporate names and logos may overshadow essential information. In addition, similar vial cap and label colors may make different products look-alike, especially if they have similar names and dosages, are used in the same setting, and/or are stored near one another. Complicating the situation, humans tend to see what they expect to see, rather than what is actually there (confirmation bias).

While prospective analysis of the package and label is a must prior to market launch, often this review is conducted with flat two-dimensional proofs that may be larger than the size of the actual label/product. Thus, vulnerabilities that may lead to a mix-up with another product may not be noticed prior to US Food and Drug Administration (FDA) approval. For this reason, ISMP recommends that healthcare organizations establish a process to ensure that all new products are evaluated by practitioners who may use them, looking at the actual packages in their work environment before drugs are added to inventory. If look-alike problems are identified, the product should be purchased from a different manufacturer if possible, or steps to catch or avoid a mix-up should be implemented (e.g., barcode scanning, separate storage, warning labels) before the drug is dispensed or administered. For more information, see our article, *Safety considerations during expedited product approval*, published in the April 6, 2023, issue.

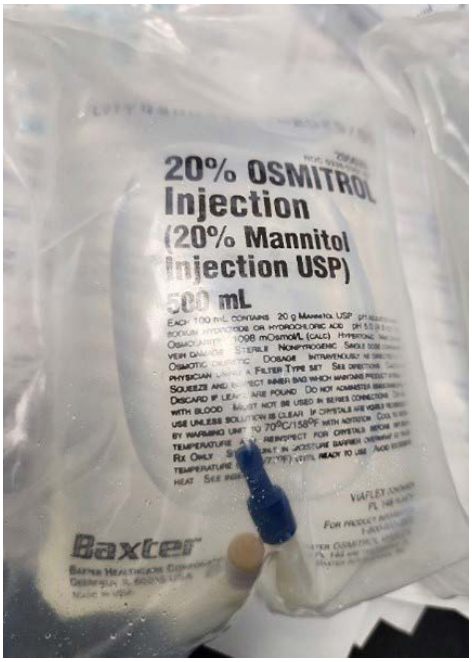

Figure 3. This infusion bag of 20% Osmitrol (mannitol) injection 500 mL does not have a barcode.

Manufacturer-Related Issues

Perhaps the most disturbing finding was that 43.2% of the events involved manufacturer-related issues: 13.3% were related to manufacturer/labeler issues; 7.5% involved manufacturer product quality issues; 6.7% involved confusing/incomplete information (label/labeling); 5.2% involved poor label design (label misleading or difficult to read);

continued on page 3 — Manufacturer labeling/quality issues >

>SAFETY briefs

cont'd from page 1

and before starting the infusion. During orientation and ongoing training, review the organization's policy and stress the need to trace infusion lines. Practice tracing lines during periodic simulations. Share impactful stories and recognize staff for good catches, including those caught through tracing the infusion line.

Topical agent packaged similarly to an injectable vial. Practitioners have reported concerns with the packaging of **MURI-LUBE** (light mineral oil), a sterile mineral oil lubricant for surgical instruments. The manufacturer, Fresenius Kabi, supplies it in a 2 mL flip, tear-top vial and a 10 mL aluminum tear-top vial (**Figure 1**) that resembles a parenteral injection vial. The vial label contains the statement "NOT FOR PARENTERAL USE"; however, practitioners may overlook this, given it resembles a parenteral injection vial. Topical product packaging that encourages practitioners to use parenteral syringes to prepare the dose risks the potential of inadvertent intravenous (IV) administration and presents a significant patient safety risk.

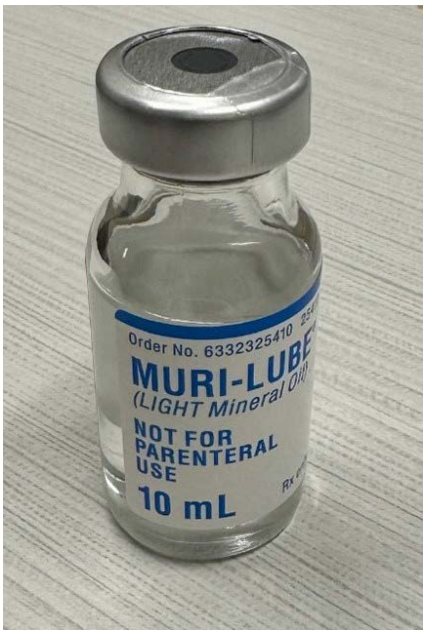

Figure 1. Muri-Lube topical agent used for surgical instrument lubrication is provided in a vial that resembles those used for parenteral injections.

We have warned about the use of negative statements on products in our August 12, 2010 article, *Affirmative warnings (do this)*

continued on page 3 — >SAFETY briefs >

> **Manufacturer labeling/quality issues** — continued from page 2

4.2% involved poor packaging design; 3.3% involved a dispensing device issue; and 3% involved poor product design (e.g., vial, syringe, bag). These obstacles often set up practitioners for errors. For example, practitioners may be forced to employ workarounds such as when a barcode is hidden or damaged, is difficult to scan (e.g., white print on clear bag), or is missing. Unsafe practices include administering a medication even though the barcode will not scan, scanning after the medication has been administered, or scanning barcodes from sources other than the medication itself (i.e., proxy scanning), such as scanning a barcode that is not affixed to the product actually being administered.

In one case, a hospital reported that they received three 500 mL bags of 20% **OSMITROL** (mannitol) injection by Baxter that did not have barcodes (**Figure 3**, page 2).

Multiple hospitals have reported the inability to scan a medication barcode due to an overwrap seam centered over the barcode on an infusion bag (**Figure 4**). The overwrap obscures the white ink barcode on the heparin sodium 25,000 units/250 mL infusion bag made by B. Braun. Since removing the bag from the overwrap shortens the beyond-use date of the product, many hospitals store it in the overwrap until right before use. The reporting hospitals are concerned that without being able to scan the barcode when dispensing or restocking ADCs, this situation increases the potential for errors with this high-alert medication.

Figure 4. The barcode that identifies B. Braun's heparin 25,000 units/250 mL is under a crimped seam on the clear overwrap, making it impossible to scan the barcode without first removing the bag.

In another case involving heparin, a hospital reported that the label on a Pfizer heparin 25,000 units/250 mL infusion bag was missing the medication name and concentration (**Figure 5**).

In another case, an organization reported that they received a carton of succinylcholine 200 mg/10 mL vials made by Meitheal, but 4 of the 25 vials did not have medication labels (**Figure 6**, page 4). The only indication of the vial contents was the cap which states, "WARNING: PARALYZING AGENT." The reporting organization was concerned that this high-alert neuromuscular blocking agent could be mistaken as a diluent vial or another medication.

Figure 5. A heparin 25,000 units/250 mL bag (Pfizer) was missing the medication name and concentration (left), which is typically displayed on the top of the heparin bag in red font (right).

Call to Action

ISMP's subsidiary, Med Safety Board (MSB), has issued a white paper calling for pharmaceutical manufacturers to ensure injectable medication labels are well-differentiated to minimize mix-ups and prevent patient harm. The

continued on page 4 — **Manufacturer labeling/quality issues** >

>SAFETY briefs

cont'd from page 2

may be better understood than negative warnings (do not do that). The concern with negative warning statements is that the practitioner may only see the active action and miss the "NOT" in the beginning part of the statement, especially if the vial is turned, the label is obstructed, or the statement is separated on to two lines. Labeling with "FOR TOPICAL USE ONLY" is recommended instead of "NOT FOR PARENTERAL USE."

We have reached out to the US Food and Drug Administration (FDA) and Fresenius Kabi and recommended modifying the packaging to a container practitioners would expect for a topical agent (e.g., tube, jar), rather than a vial that resembles an injectable medication. If the package cannot be changed, we recommend the manufacturer improve the warning statement on the label.

If your organization purchases this product, ensure staff are aware of the appropriate preparation and use of this product. Apply auxiliary labels to vials and storage areas that clearly indicate the product is for topical use for surgical instrument lubrication. Do not store Muri-Lube next to mineral oil products intended for oral or rectal use. Report close calls and errors to your organization's error reporting program and ISMP.

Budesonide prescribed instead of bumetanide results in readmission. A patient with congestive heart failure was hospitalized for fluid overload. A medical resident intended to prescribe oral bumetanide 6 mg (requiring the patient to take 3 of the 2 mg oral tablets) once a day at home. When the resident entered the prescription in the electronic health record (EHR), the screen allowed him to search for the medication name using only two letters. He inadvertently selected and prescribed budesonide 6 mg (requiring the patient to take 2 of the 3 mg delayed-release capsules) orally once a day. The prescription did not include an indication, and the outpatient pharmacy dispensed budesonide. The patient took the incorrect medication for five weeks before they were readmitted to the hospital for fluid overload and the error was discovered.

continued on page 4 — >SAFETY briefs >

> **Manufacturer labeling/quality issues** — continued from page 3

white paper includes key labeling attributes that manufacturers should consider when designing labels and healthcare organizations should consider when purchasing or adding products to their formulary or changing to another manufacturer of a formulary drug because of a shortage.

The FDA barcode rule (21 CFR 201.25) requires most prescription drugs to have a linear barcode on the label that contains, at a minimum, the drug's national drug code (NDC) number. The linear barcode must appear on the label as defined by section 201(k) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) meaning that FDA intends for the linear barcode to be on the outside container/wrapper, as well as on the immediate container, unless the barcode is readily visible and machine-readable through the outside container/wrapper. The linear barcode must also be surrounded by sufficient blank space so it can be scanned correctly. However, we continue to receive reports where drug manufacturers failed to meet this basic requirement.

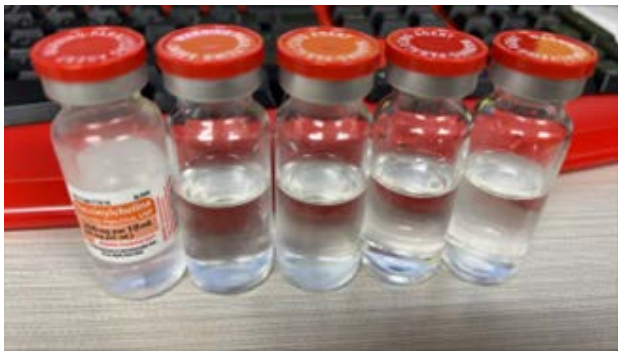

Figure 6. A practitioner found that 4 of the 25 vials in a carton of Meitheal's succinylcholine were unlabeled.

We urge the FDA and manufacturers to act and take steps to ensure better differentiation of similar-looking packaging and labeling. Manufacturers must address quality-related issues that often lead to the inability of practitioners to scan medication barcodes. The errors reported often involve high-alert medications that have the potential to harm patients.

Conclusion

The ISMP MERP provides a rich resource for learning and educating about medication errors. Your willingness to voluntarily report medication errors and hazards to ISMP and to proactively use the information we publish in the newsletter to prevent similar errors and hazards, motivates and inspires us as, together, we can continue to learn about the causes of medication errors and how to prevent them. We extend our sincere thanks to those who have submitted reports to the ISMP MERP and we encourage all of our readers to continue these efforts.

Special Announcement

ISMP survey on parenteral nutrition (PN)

We are conducting a short survey about PN including the use and safety of multi-chamber bag parenteral nutrition (MCB-PN) and patient-specific compounded (i.e., custom) PN. Please take 10 minutes to complete this survey by **January 23, 2025**. We appreciate your participation!

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Report medication and vaccine errors to ISMP: Please visit www.ismp.org/report-medication-error or call 1-800-FAIL-SAF(E). ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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>*SAFETY* briefs

cont'd from page 3

If only a portion of the name is used to search for products or populate fields in the EHR or prescription ordering systems, consider requiring the entry of a minimum of the first five letters of the drug name. Of course, it is best to keep adding letters until the intended drug name appears distinct by itself. Prescribers should include the purpose of the drug on prescriptions to help ensure the correct medication is selected. Pharmacists should review the prescription label with the patient, confirm the indication, and ensure it is the medication they expect.

Vaccine registry not checked before administration. A nurse administered **TYPHIM VI** (typhoid vi polysaccharide vaccine) 0.5 mL injection to a clinic patient. When documenting the vaccine administration in the state immunization information system (registry), the nurse saw that the patient had previously received **VIVOTIF** (typhoid vaccine live oral Ty21a) capsules. Therefore, the patient should not have been reimmunized against typhoid fever for five years. The prescriber and patient were notified, and no harm was reported.

The ISMP ***Targeted Medication Safety Best Practices for Hospitals*** *Best Practice* #22, recommends safeguarding against errors with vaccines administered in the inpatient and associated outpatient settings. This includes verifying a patient's immunization status in the electronic health record [EHR] as well as immunization information system (registry) prior to providing vaccines. Provide vaccinators with ongoing education and competency assessments, including the need to verify immunization status in information systems **prior to** administration, as this can identify wrong timing errors (e.g., interval too short) before reaching the patient. Encourage staff to share close calls and report vaccine errors internally as well as to ***ISMP National Vaccine Errors Reporting Program*** (ISMP VERP), and the Vaccine Adverse Event Reporting System operated by the US Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC).

Special thanks to our 2024 MSOS Member Briefings Presenters

The Medication Safety Officers Society (MSOS) holds *Member Briefings* every other month on various medication safety topics. The MSOS *Member Briefings* are webinars that feature three 10-minute presentations from volunteer MSOS members who highlight a project, initiative, or relevant medication safety topic. The goal is for participants to take the information presented and use it to implement similar medication safety initiatives within their own organization. At each *Member Briefing*, ISMP President Rita Jew also provides an update on ISMP activities. Please let us know (ismpinfo@ismp.org) if there is a medication safety topic you would like to present (or see presented) during a 2025 MSOS *Member Briefing*. We hope others can join us as presenters in 2025! To join the MSOS and attend the *Member Briefings*, visit: www.medsafetyofficer.org/user/register. MSOS membership and the 2025 *Member Briefings* are **FREE**.

Production of the MSOS *Member Briefings* would not be possible without the assistance of voluntary MSOS member presenters. ISMP sincerely thanks MSOS *Member Briefings* moderator Bob Feroli, PharmD, FASHP and all of the 2024 presenters sharing their knowledge and expertise in pursuit of our mission to advance and encourage excellence in medication use safety.

Thank You!

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