July 30, 2020 ■ Volume 25 Issue 15

ISMP
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Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Survey shows room for improvement with two new ISMP Targeted Medication Safety Best Practices

In our February 27, 2020 newsletter, we invited hospitals to participate in a short survey to establish a baseline level of implementation for two new Best Practices released in the ***2020-2021 ISMP Targeted Medication Safety Best Practices for Hospitals*** (www.ismp.org/node/160). The purpose of the ***Targeted Medication Safety Best Practices*** is to identify, inspire, and mobilize widespread, national adoption of consensus-based Best Practices to address recurring problems that continue to cause harmful and even fatal errors despite repeated warnings in ISMP publications. The two new Best Practices for 2020-2021 are associated with safely prescribing extended-release (ER) and long-acting (LA) opioids and minimizing the use of the override feature when accessing medications in automated dispensing cabinets (ADCs).

The survey was initially scheduled to end on April 17, 2020. However, the window of opportunity to participate was extended until July 17, 2020, because many US hospitals were operating at full capacity and above during the early stages of the coronavirus (COVID-19) pandemic. While the overall response to this survey is less than with past ISMP surveys, and any delay in implementation of the new Best Practices is understandable during the pandemic, we want to sincerely thank the hospitals that participated in the survey and share the valuable lessons learned from the findings. An overview of the survey findings is presented in **Table 1** (page 4) and detailed below.

Respondent Profile

Almost 250 (N = 247) US hospitals participated in our survey. More than a quarter (28%) of the responding hospitals were licensed for 500 beds or more; 18% had 300-499 beds; 27% had 100-299 beds; and 27% were smaller hospitals with 26-99 beds (15%) or 25 beds or less (12%). Overall, more than half (58%) of the hospitals reported employing one or more part- or full-time medication safety officer(s). The percentage of responding hospitals with a medication safety officer rose steadily as bed size increased, ranging from 25% in smaller hospitals with less than 100 beds to 85% in larger hospitals with 500 beds or more. With few exceptions, hospitals with a medication safety officer tended to report higher levels of implementation of the two new Best Practices. There were also differences in reported implementation levels based on bed size, as described below.

New Best Practice #15: Safe Opioid Prescribing

New Best Practice #15 comprises five interventions designed to improve safe prescribing of ER and LA opioids. The first intervention recommends verifying and documenting the patient's opioid status (naïve versus tolerant) and type of pain (acute versus chronic) before prescribing and dispensing ER or LA opioids. Only 15% of hospitals reported full implementation of this intervention; 44% reported partial compliance; and 41% reported no implementation. Full implementation was greatest in hospitals with 26-99 beds (31%). Most reported barriers to implementation focused on limitations in the electronic health record (EHR), such as the inability to add a hard stop, alert, or mandatory field for the documentation of opioid status. Some respondents noted that documentation of opioid status is only required for certain opioids such as fenta**NYL** patches, patient-controlled analgesia (PCA), or large doses of ER and LA opioids. Many reported relying on pharmacists to evaluate the patient's opioid status during order verification.

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SAFETY briefs

Can a product have two different expiration dates? Apparently so. An expiration date printed on a prefilled syringe of **DEPO-PROVERA** (medroxy-**PROGESTER**one) by Pfizer (**Figure 1**) did not match the expiration date on the outer carton containing the syringe. The expiration date listed on the outer carton was earlier. A company representative said that the product has two separate components: a drug syringe and a 22-gauge, 1½ inch needle for deep intramuscular (IM) injection. The two components may have different manufacturer expiration dates. Each assembled syringe and needle is packaged in an individual

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Figure 1. Expiration date (August 31, 2024) on Depo-Provera syringe does not reflect the actual expiration date of the assembled syringe and needle; the expiration date on the carton (October 31, 2023) is correct.

ISMP survey on pharmacy compounding

If you are a **pharmacist or pharmacy technician** who prepares or oversees the production of compounded sterile preparations (CSPs), please take our survey on pharmacy compounding by **September 18, 2020**, at: www.ismp.org/ext/526. A copy of the survey questions appear on **pages 5** and **6.** While compounding sterile preparations requires following standards to ensure sterility and stability of the final product, steps must also be taken to identify, reduce, and eliminate errors and their causative factors to minimize the risk of patient harm. Please help ISMP learn more about compounding practices by completing our survey!

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The next intervention recommends defaulting order entry systems to the lowest initial starting dose and frequency when initiating orders for ER and LA opioids. Less than one-quarter (23%) of hospitals reported full implementation; 30% reported partial compliance; and almost half (47%) reported no implementation. Full implementation was greatest in hospitals with 26-99 beds (27%).The most prevalent barrier reported was EHR limitations, and many respondents noted that their EHR currently presents all opioid dosage strengths from lowest to highest. Some hospitals reported physician resistance, while others reported defaulting to zero or the most commonly prescribed dose (which may not be the lowest starting dose). A few respondents reported low compliance with using opioid order sets or templates, nullifying the error-reduction impact of embedded dosing defaults.

The third intervention recommends alerting practitioners when ER and LA opioid dose adjustments are required due to age, renal or liver impairment, or when patients are prescribed other sedating medications. Less than one-quarter (24%) of hospitals reported full implementation; 40% reported partial compliance; and more than one-third (36%) reported no implementation. Smaller hospitals tended to report full implementation of this intervention more frequently than larger hospitals. Most respondents who have not implemented this intervention rely on pharmacists to intervene with dose adjustments during order verification. Respondents who reported partial compliance noted that drug-drug interaction alerts (for concomitant sedating agents) were more common, and renal or hepatic dosing alerts were least common. A few respondents expressed concerns about alert fatigue, overridden alerts, and EHR limitations with creating these alerts.

The fourth intervention recommends eliminating the prescribing of fenta**NYL** patches for opioid-naïve patients and/or patients with acute pain. Forty-one percent of hospitals reported full implementation of this intervention; 37% reported partial compliance; and almost one-quarter (22%) reported no implementation. Full implementation was greatest in hospitals with 300 beds or more (53%). Among hospitals that have not implemented this intervention, more than half reported they were either depending on alerts to warn prescribers about inappropriate prescribing or depending on pharmacists to intervene during verification. Several respondents reported that pharmacists have difficulty determining the appropriateness of fenta**NYL** patches because the patient's opioid status is not known or documented, and that prescribers are sometimes confused regarding the criteria to determine opioid tolerance. A few respondents reported exceptions for palliative and end-of-life care.

The last intervention with Best Practice #15 recommends eliminating the storage of fenta**NYL** patches in ADCs or as unit stock in clinical locations where acute pain is primarily treated (e.g., emergency departments [EDs], operating rooms, post-anesthesia care units, procedural areas). Almost three-quarters (71%) of hospitals reported full compliance with this intervention; 15% reported partial compliance; and 14% reported no compliance with this intervention. Few barriers to implementation were reported, and those with partial compliance mostly reported that the patches remained in stock in the ED, sometimes for patients who were awaiting inpatient admission.

New Best Practice #16: Minimizing Use of the ADC Override Feature

New Best Practice #16 comprises five interventions designed to minimize the use of the override feature when accessing medications in ADCs. "Override" refers to the process of bypassing the pharmacist's review of a medication order to obtain a medication from the ADC when assessment of the patient indicates that a delay in therapy would harm the patient. The first intervention recommends limiting the variety of medications that can be removed from an ADC using the override function. More than half (59%) of hospitals reported full implementation; 32% reported partial compliance; and 9% reported no compliance with this intervention. Full implementation was greatest in hospitals with 100 or more beds (66%). Among respondents reporting partial implementation, the most common barrier was that the pharmacy was not open 24 hours and did not employ

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carton. Therefore, when assigning an expiration date to the combined product, the manufacturer uses the earlier of the two expiration dates and prints that date on the carton. According to the manufacturer, the date printed on the outer carton of the combination pack is the actual expiration date.

HIGH-ALERT

FDA revises labeling for methotrexate tablets. The US Food and Drug Administration (FDA) has revised the labeling for methotrexate (www.ismp.org/ext/523), removing the option of administering weekly doses of the medication in divided doses given every 12 hours for 3 doses. In the past, ISMP has received reports about fatal errors in which a patient misunderstood those directions on their prescription container and took, for example, methotrexate 2.5 mg every 12 hours over several consecutive days, instead of 2.5 mg every 12 hours for 3 doses each week.

For non-oncologic indications, the recommended starting dose of methotrexate tablets is: 1) 7.5 mg orally once weekly for rheumatoid arthritis, with escalation to achieve optimal response; 2) 10 mg to 25 mg orally once weekly for psoriasis until adequate response is achieved; and 3) 10 mg/m^2 orally once weekly for pediatric patients with polyarticular juvenile idiopathic arthritis, with dose adjustments to achieve an optimal response. There is an exception to once weekly dosing for certain cancer patients. Dosing for patients with refractory or relapsed non-Hodgkin lymphomas is 2.5 mg orally two to four times per week as part of metronomic combination chemotherapy. Also, to treat mycosis fungoides, the recommended dose is 25 mg to 75 mg orally once weekly as monotherapy or 10 mg/m^2 orally twice weekly as part of combination therapy.

Methotrexate product labeling notes that recommended dosing should be reinforced with patients and caregivers because taking weekly doses daily has led to deaths. ISMP believes these changes are an important step forward in preventing medication errors caused by dosing confusion. Please make all appropriate clinical staff in your organization aware of this change and be sure any printed medication information you provide to patients reflects this change.

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remote order entry verification (requiring override access to medications in the ADC). Hospitals also reported specific locations, such as the ED and perioperative areas, where overrides occurred frequently. Most respondents who reported partial implementation felt their list of medications available via override could easily be pared down.

The next intervention recommends requiring a medication order (e.g., electronic, written, telephone, verbal) prior to removing any medication from an ADC, including those removed via override. Half (50%) of hospitals reported full compliance with this intervention; 32% reported partial compliance; and 18% reported no implementation of this intervention. Full implementation was greatest in hospitals with 100-499 beds (61%). Respondents reporting partial compliance frequently noted the presence of a policy that required an order prior to ADC removal of medications but said the policy is not always followed. Barriers to implementation included cultural issues and misperceptions that the removal of medications from an ADC alone serves as orders in perioperative and procedural areas. Several hospitals that reported full compliance told us that retrieving a medication from an ADC via override without an order is considered a medication error.

The third intervention recommends monitoring overrides to verify appropriateness, transcription of orders, and documentation of administration. Approximately half (53%) of hospitals reported full implementation; 44% reported partial compliance; and 3% reported no compliance. Full implementation was greatest in hospitals with 26-99 beds (92%). Hospitals reporting partial compliance said they are monitoring overrides only for controlled substances or other targeted or randomly selected medications due to time constraints. Some respondents also noted that overrides are only reviewed for a corresponding order and documentation of administration, not the appropriateness of the override.

The fourth intervention recommends periodically reviewing for appropriateness the list of medications available using the override function. Two-thirds (67%) of hospitals reported full compliance with this intervention; 25% reported partial compliance; and 8% reported no compliance. Few barriers were reported, and most respondents reporting full compliance said they reviewed lists annually.

The last intervention recommends restricting medications available via override to those that would be needed emergently (organization-defined) such as antidotes, rescue/reversal agents, life-sustaining drugs, and comfort measure medications (e.g., for acute pain, intractable nausea/vomiting). More than half (56%) of hospitals reported full compliance with this intervention; 37% reported partial compliance; and 7% reported no compliance. Full implementation was greatest in hospitals with 100 or more beds (61%). Respondents who reported partial compliance noted that additional access to medications in ADCs was required when the pharmacy was closed. A few respondents reported resistance to limiting access in certain locations, including the ED. Several respondents told us about low-risk medications that had been made available via override to facilitate throughput in the ED and perioperative locations.

Conclusion

These survey results suggest there is sizeable room for improvement during 2020-2021 with the two new Best Practices associated with safe opioid prescribing and minimizing ADC overrides. We hope that hospitals will take note of the barriers and misperceptions that may delay implementation of these important safety strategies, and use the survey results to prompt interdisciplinary discussions about potential barriers to implementation along with brainstorming ways to resolve them.

For example, a discussion about Best Practice #15 might lead to the discovery of the best process to collect and document the opioid status of patients. Some providers ask all new patients about opioid use (including heroin and/or non-prescribed opioids) during the past few weeks and make an initial determination of opioid status when creating a home medication list, which is verified upon medication reconciliation and documented

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Also, implement a weekly dosage regimen default for oral methotrexate and a hard-stop verification of an appropriate oncologic indication for all daily oral methotrexate orders, as described in Best Practice #2 in the ***2020-2021 ISMP Targeted Medication Safety Best Practices for Hospitals*** (www.ismp.org/node/160).

Corlanor oral solution now available to hospitals. Ivabradine (**CORLANOR**) is approved for the treatment of stable symptomatic heart failure due to dilated cardiomyopathy (DCM) in pediatric patients aged 6 months and older, who are in sinus rhythm with an elevated heart rate. To ensure it is effective and well tolerated before an outpatient prescription is written, the drug may be started in the hospital. The drug is available in 5 mg and 7.5 mg tablets, as well as an oral solution of 5 mg/5 mL. However, until recently, hospitals could only purchase the product in tablet form, and the oral solution was only available through a single specialty pharmacy, Avella, which would not dispense the drug to hospitals.

The recommended starting dose for children 6 months and older and weighing under 40 kg is just 0.05 mg/kg twice daily. Without an oral solution available, the hospital pharmacy was required to compound liquid doses needed for children using tablets. For a 10 kg patient, the dose is just 1/10 of a tablet. A 20 kg child would need just 1 mg or 20% of the tablet strength. To measure an appropriate dose, the full tablet had to be crushed and mixed in water, and only a portion of the final mixture given to the patient. As you can imagine, this introduced the risk for dosing errors. A pediatric hospital had several instances where patients received overdoses because the full crushed tablet was administered in error.

These events could easily be prevented if hospitals were able to purchase the oral solution. We contacted the product manufacturer, Amgen, to clarify why Corlanor oral solution was in limited distribution through a specialty pharmacy, impeding access by hospitals and increasing the risk of medication errors. We learned that the company has recently made the oral solution available to hospitals through Cardinal Health (hospitals and 340B pharmacies can call 855-855-0708; primary care providers can call 877-453-3972).

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on the patient's medication list or in the EHR. Other providers require a determination of opioid status per established criteria with all opioid pain management order sets, which guide the selection and dosing of opioids. An interdisciplinary discussion about Best Practice #16 might lead to a requirement to document the rationale for any overrides, ADC screen changes to facilitate this process, the development of criteria to monitor the appropriateness of all ADC overrides, the adoption of remote pharmacy order verification when the pharmacy is closed, the use of profiled ADCs in all clinical areas, and the commission of an interdisciplinary group to routinely analyze all (not just controlled substances) override reports to identify if an order was obtained prior to removing the medication and whether the rationale for each overridden medication was appropriate.

The basis for recommending the two new Best Practices, along with related ISMP publications and guidelines for additional information, can be found in the full ***2020-2021 ISMP Targeted Medication Safety Best Practices for Hospitals*** (www.ismp.org/node/160). An Implementation Worksheet (www.ismp.org/node/1506) for all of the Best Practices is also available and might be helpful.

Table 1. Compliance with two new ***2020-2021 ISMP Targeted Medication Safety Best Practices for Hospitals***

Best Practice		Compliance (%)			Common Barriers/Comments
		None	Partial	Full	
#15	Verify/document a patient's opioid status (naïve vs. tolerant) and type of pain (acute vs. chronic) before prescribing/dispensing ER/LA* opioids	41	44	15	EHR† limitations (e.g., no hard stop, no mandatory field); only required for fenta**NYL** patches
	Default order entry systems to the lowest initial starting dose and frequency for ER/LA* opioids	47	30	23	EHR† limitations; physician resistance; dosage strengths presented from lowest to highest
	Alert practitioners when ER/LA* opioid dose adjustments are required (age, renal/liver impairment, other sedating medications)	36	40	24	Relying on pharmacy interventions; EHR† limitations; concern about alert fatigue
	Eliminate fenta**NYL** patch prescribing for opioid-naïve patients/patients with acute pain	22	37	41	Relying on pharmacy interventions or prescriber alerts; exceptions for palliative or end-of-life care
	Eliminate storage of fenta**NYL** patches in locations where acute pain is primarily treated	14	15	71	Stored in the ED,‡ sometimes for patients awaiting inpatient admission
#16	Limit the variety of medications that can be removed from an ADC§ via override	9	32	59	Pharmacy not open; exceptions in the ED‡ and perioperative areas
	Require an order prior to removing medications from an ADC§ (including via override)	18	32	50	Policy not always followed; ED‡ and perioperative areas not compliant
	Monitor ADC§ overrides to verify appropriateness, order transcription, documentation of administration	3	44	53	Mostly monitoring controlled substances and/or targeted medications; no criteria for monitoring appropriateness
	Periodically review for appropriateness the list of medications available via override	8	25	67	Most reviews occur annually; no standard process to review appropriateness
	Restrict medications available via override to those that would be needed emergently	7	37	56	Exceptions for low-risk medications; no restrictions when pharmacy closed; resistance in the ED§

*ER = extended-release, LA = long-acting; †EHR = electronic health record; ‡ED = emergency department; §ADC = automated dispensing cabinet

Special Announcements

FREE international ISMP webinars

ISMP is presenting two FREE webinars intended for an international audience:

August 18: ***A Look Behind the Scenes: Global Progress in Patient Safety and Prevention of Harmful Medication Errors***

September 15: ***Enhancing Your Medication Error Reporting Program to Improve Global Medication Safety***

On **August 18**, join us in looking back at medication safety progress that has been made and looking forward to areas that require improvement. To register, visit: www.ismp.org/node/18844. On **September 15**, learn how to improve practitioner reporting and apply ISMP's system-based approach to error analysis. To register, visit: www.ismp.org/node/19035.

Don't miss ISMP's virtual mentoring

Spend a week, **August 17-21, 2020**, in live, online mentoring sessions with the nation's top medication safety leaders through ISMP's virtual **Practitioner in Residence** program—no travel required! Participants will learn to use ISMP's unique model for identifying and controlling risk exposure and gain insights on contemporary safety challenges. The number of participants is limited to allow for dedicated attention to your safety learning needs. To learn more or enroll, visit: www.ismp.org/node/19224.

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

ISMP Survey on Pharmacy Sterile Compounding

If you are a **pharmacist or pharmacy technician who prepares or oversees the production of compounded sterile preparations** (CSPs), please take our survey on pharmacy compounding! While compounding sterile preparations requires staff to follow standards to ensure sterility and stability of the final product, steps must also be taken to identify, reduce, and eliminate errors and their causative factors to minimize the risk of patient harm. You can help ISMP learn more about safe compounding practices, available pharmacy compounding technologies, and compounding errors by completing our survey by **September 18, 2020**, which can be found at: www.ismp.org/ext/526.

This survey is focused on pharmacy compounding. In the future, ISMP plans to conduct a related survey on compounding and admixture performed outside of the pharmacy.

Safe Compounding Practices

1 Please tell us the degree of implementation with the following safe compounding practices or conditions, considering all times/shifts throughout the day.

Key: **Never** = 0% of the time **Rarely** = 1 to 10% of the time **Sometimes** = 11 to 50% of the time
Often = 51 to 95% of the time **Always** = greater than 95% of the time

Best Practice or Condition	Degree of Implementation					Comments
	Never	Rarely	Some-times	Often	Always	
a) There is sufficient counterspace to gather and stage each component needed to prepare CSPs without the risk of intermingling/overlapping or the need to stage/store items on top of one another.						
b) During the verification process, it is easy to identify without uncertainty which drugs, diluents, and volumes were used (including the number of vials/ampules/bags used) to prepare each CSP.						
c) Bins are used during the compounding of each CSP (or each batch of identical preparations) to permit segregation (separation) from other CSPs.						
d) Only one CSP is prepared in a workbench/laminar flow hood/biological safety cabinet at a time.						
e) There are enough workbenches in the cleanroom/sterile compounding area to support only 1 staff member working at a time per primary engineering control device (e.g., laminar airflow workbench, biological safety cabinet, isolator).						
f) Standard operating procedures are defined and utilized by all staff during the compounding process.						
g) Standard operating procedures are defined and utilized by all staff during the verification/checking process for CSPs.						
h) Lighting and noise in all locations where CSPs are prepared and verified have been measured (e.g., lux, foot-candle, dBA) and is consistent with standards (e.g., USP: 1,000-1,500 lux, 50 dBA).*						
i) A standard workflow is followed for how final product labels are placed onto CSPs (e.g., location, flagging, label orientation).						
j) When compounding a CSP, dose volume information is available on a preparation label, master formula record, or other approved document, so there is no need for calculations.						

Compounding Technologies

2 When you compound sterile preparations, do you use compounding technologies?
☐ Yes ☐ No (skip to question #5)

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3 Please tell us which compounding technologies are used and the percent of CSPs prepared using these technologies.

Compounding Technology	Yes	No	% of CSPs Prepared	Comments
a) IV sterile compounding robot				
b) Workflow system that uses barcode **and** gravimetric verification and images				
c) Workflow system that uses barcode verification and images				
d) Barcode verification **without** images				
e) Image sharing or remote video supervision				
f) Automated multiple ingredient compounding device (e.g., parenteral nutrition compounders)				

4 If you use compounding technology that utilizes images to verify CSPs, are there any medications which you verify prior to completion of all compounding steps (e.g., does production stop for verification of the drug, diluent, and dose before compounding is complete)? ☐ No
☐ We do not use compounding technology that ultizes images
☐ Yes. If yes, which medications? _____
☐ No

Sterile Compounding Errors

5 Are you aware of any pharmacy sterile compounding errors **during the past 12 months**, including both those caught and corrected in the pharmacy, as well as those discovered after dispensing?
☐ Yes. Please specify the error type(s) (select all that apply) ☐ No
- ☐ Issues, errors, and omissions with labeling CSPs
- ☐ Incorrect base solution
- ☐ Incorrect base solution volume
- ☐ Incorrect drug
- ☐ Omission of a drug
- ☐ Incorrect dose or concentration
- ☐ Incorrect reconstitution of a drug (volume or diluent)
- ☐ Wrong preparation technique (e.g., improper filtering, wrong tubing)
- ☐ Wrong timing (e.g., chemotherapy prepared on the wrong date)
- ☐ Expired drug vial, base solution, or CSP
- ☐ Error with solutions from 503B pharmacies used for pharmacy compounding
- ☐ Other (please specify):_____

6 What is the biggest safety challenge or other concerns/comments you have related to pharmacy sterile compounding?

_____

About Your Facility and You

7 Does your pharmacy prepare non-sterile to sterile compounded preparations?
☐ Yes. If yes, what percent of all CSPs are non-sterile to sterile? _____
☐ No

8 Is your facility registered as a 503B compounding pharmacy?
☐ Yes ☐ No

9 Please select the categories that best describe your profession, current position, and work setting:
Profession: ☐ Pharmacist ☐ Pharmacy technician ☐ Other (please specify):_____
Position: ☐ Staff ☐ Manager/Director ☐ Administrator ☐ Other (please specify):_____
Work setting: ☐ Hospital ☐ Ambulatory infusion center ☐ Outpatient/compounding pharmacy ☐ Other (please specify):_____

*USP. <1066> - Physical environments that promote safe medication use. October 1, 2010. www.ismp.org/ext/525