June 2023 | Volume 22 ■ Issue 6

ISMP
An ECRI Affiliate

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

Design systems to manage REMS programs and maximize their potential to reduce the risk of errors

Problem: Risk evaluation and mitigation strategies (REMS) programs were first instituted by the US Food and Drug Administration (FDA) in 2007 to ensure the benefits of a medication with serious safety concerns outweigh the risks.[1] REMS programs include one or more of the following components designed to reinforce medication-use behaviors and actions that support safe use: (1) Patient information (e.g., *Medication Guide*), (2) Communication plan, (3) Elements to assure safe use (ETASU), and (4) Implementation system. ETASU may include certification of prescribers or dispensers, drug administration being restricted to certain healthcare settings, specific monitoring requirements for patients, or enrollment of patients in a registry.[2,3] REMS programs also have a timetable of assessments of when the manufacturer will provide reports to the FDA to evaluate the effectiveness of the REMS components.[1,2]

There are approximately 60 medications that currently have REMS requirements. In December 2021, FDA launched the REMS Public Dashboard (www.ismp.org/ext/1112) to expand efficient access to data and report-generating capabilities of REMS programs for healthcare providers, research organizations, academia, industry, and others.

While REMS programs are intended to mitigate risk, the number of different programs and databases, wide variety of program requirements, scarcity of implementation tools, and lack of organizational resources may make it difficult for frontline practitioners to meet the requirements of the various programs. Pharmacies and medical offices may face other challenges, some of which are highlighted below, based on reports we have received.

REMS-related problems reported to ISMP

Dispensing to the patient instead of the provider. A specialty pharmacy reported an error in which **SPRAVATO** (esketamine) was accidentally shipped to the patient directly instead of to the provider. Spravato is used for treatment-resistant depression in adults, and it is only available through a REMS program that requires certification of dispensing pharmacies and treatment facilities as well as enrollment of patients. It is supplied as a nasal spray device that is to be administered under the direct supervision of a healthcare provider. It should never be dispensed directly to a patient for use at home. Thankfully, the patient knew that they should not self-administer this medication and that it should be administered at the provider's office, so they did not attempt to take the medication themselves.

The reporting pharmacy confirmed that they had processes designed to ship Spravato to the provider instead of the patient; however, breakdowns occurred. The specialty pharmacy identified a number of factors that contributed to this error:

- The pharmacy was managing significant staff turnover, making it difficult to keep all staff up-to-date on REMS requirements. On the day of this event, the pharmacy was also short-staffed and experiencing high prescription volume.
- Although alerts fire in the dispensing system when a medication must be delivered to a clinic or medical office, these alerts appear with other alerts (e.g., clinical, drug utilization review [DUR]) and can be missed. Also, alert fatigue was identified as a contributing factor.

continued on page 2 — REMS programs >

SAFETY briefs

Educate patients about DisposeRx packets. DisposeRx packets are intended for use by patients and caregivers at home to enable the safe disposal of unused or expired medications. These packets may be provided by the pharmacy when dispensing prescriptions and can be used with a variety of medication formulations, including oral solids, liquids, and powders. The DisposeRx packets contain a mixture of solidifying materials in powder form. When water and the DisposeRx powder are added to medications in a prescription bottle and then shaken, the drugs become chemically and physically sequestered in a

continued on page 2 — SAFETY briefs >

Welcome to Jen, our newest ISMP staff member!

We are pleased to announce that **Jennifer Young**, PharmD, BCPS, CSP has joined ISMP as a Medication Safety Specialist, supporting ISMP's Specialty Pharmacy Membership and contributing to newsletters and consulting efforts, particularly in the community and specialty pharmacy practice settings. She comes to us from Atrium Health Wake Forest Baptist in NC, where she most recently served as Program Director for Specialty Pharmacy Services, including two specialty pharmacy dispensing sites (both with URAC and Accreditation Commission for Healthcare [ACHC] specialty pharmacy accreditation), a specialty pharmacy call center, clinic embedded pharmacy staff, and a medication access team. Jen received her Doctor of Pharmacy degree from the University of Georgia College of Pharmacy and completed her residency at Wake Forest Baptist Medical Center. She is a Board Certified Pharmacotherapy Specialist and a Certified Specialty Pharmacist. Please join us in welcoming Jen!

> REMS programs — continued from page 1

- The pharmacy dispensing software is designed for mail order and retail pharmacy, not specialty pharmacy. As a result, it does not have the functionality to support the specialty pharmacy workflow. For example, it does not have a specific indicator or default setting to ship a medication to the doctor instead of to the patient. To work around this, staff manually enter notes in anticipation that subsequent staff notice and act upon the notes to identify where to correctly ship the medication.

- While the pharmacy maintains a list of clinic-administered medications to help remind staff which medications should be shipped to the provider, this list is only available in a separate central file-sharing location. At the time of the error, this information or access to the resource was not readily available within the workflow and often overlooked.

Inappropriate prescribing of fentaNYL citrate oral transmucosal lozenge (ACTIQ). Actiq is indicated for the management of breakthrough pain in cancer patients 16 years and older who are opioid-tolerant. Both inpatient and outpatient pharmacies must be certified to dispense Actiq, which includes enrolling in the transmucosal immediate-release fenta**NYL** (TIRF) REMS program and training staff in the program requirements. Pharmacies must also develop policies and procedures to verify opioid tolerance or assess a change in opioid tolerant status. While outpatient pharmacies need to obtain a REMS Dispense Authorization to dispense TIRF medications, inpatient pharmacies do not. To prescribe a TIRF medication for outpatient use, prescribers must be certified within the program.

A pharmacist reported three separate occasions in which prescribers attempted to order an agent to treat sore throat, searched for "lozenge," and inadvertently prescribed Actiq. Fortunately, for two of these instances, a pharmacist identified that the patients did not have a disease state necessitating TIRF and contacted the provider for correction. On the third occasion, the prescriber immediately recognized their own error. In each of these cases, the patients had not been taking other opioids and were therefore opioid-naive. The pharmacist noted that the electronic health record (EHR) should limit the ability to prescribe TIRF products to only appropriate (for inpatient orders) and certified prescribers (for outpatient prescriptions).

Safe Practice Recommendations: Organizations such as the American Society of Health-System Pharmacists (ASHP) have advocated for a centralized electronic REMS system to help practitioners manage the need of various registrations, provider education, and patient documentation requirements (www.ismp.org/ext/1113). ISMP is in support of this statement and also calls upon EHR, pharmacy computer system, and clinical management software vendors to design systems to better manage REMS requirements. Organizations should consider the following recommendations:

Assign a REMS coordinator. Pharmacies should designate an individual responsible for identifying medications with REMS programs that are dispensed. The coordinator should be responsible for enrolling the organization in REMS programs, educating staff, and demonstrating compliance through routine audits. In addition, to ensure consistency of REMS management in the absence of the REMS coordinator, consider cross-training staff.

Assess REMS requirements upon initial addition to pharmacy inventory. Proactively conduct a risk assessment of clinical and operational requirements for REMS medications that may be prescribed and/or dispensed.

Develop a policy and procedure for REMS programs. Develop a policy outlining all medications with associated REMS programs. This policy should include educational requirements, competency assessments, and procedures for prescribing, dispensing, and administration. Document review of this policy on an annual basis. Establish criteria on where and for how long REMS compliance documentation must be maintained to meet the REMS requirements. Consider creating a REMS

continued on page 3 — REMS programs >

>SAFETY briefs

continued from page 1

viscous gel trapping the medication's active ingredients. Once the reaction is complete, the prescription bottle can be thrown away in the household trash.

However, since these packets are dispensed along with medications, there may be a risk that patients mistake the packets for a medication. That is exactly what happened in a case reported to ISMP. On a home care visit with a Spanish-speaking new mom, the home care nurse was using the language interpretation line to review the patient's medications. The patient showed the nurse all her medications including the DisposeRx packet. The patient thought it may be something that she needed to ingest. Thankfully, the home care nurse was able to intervene and the patient did not ingest the DisposeRx powder.

Pharmacies that dispense DisposeRx packets with medications should educate patients about the safe and appropriate use of these packets, making sure to alert patients that the contents are not to be ingested. In addition to the instructions in English that are printed on the DisposeRx packet, the company has made available on their website (www.ismp.org/ext/1197) instructions for use in Spanish and French. Incorporate prompts into the pharmacy computer systems to have the pharmacist provide patient education about DisposeRx. Additionally, practitioners working with home health agencies should provide education to home care nurses about these packets.

Some prefilled syringes still pose risk of needlestick injuries. In the August 2022 issue of this newsletter, we reported the potential for accidental needlestick injuries with the use of manufacturer prefilled syringes that do not come with a needle safety guard. The products mentioned included **EVENITY** (romosozumab-aqqg), **KINERET** (anakinra), and **HUMIRA** (adalimumab). We recently received a report of another prefilled syringe with the same issue—**LEQVIO** (inclisiran). Leqvio is supplied in a carton with one single-dose prefilled syringe containing 284 mg/1.5 mL

continued on page 3 — SAFETY briefs >

> REMS programs — continued from page 2

resource binder (electronic and hard copy) that staff can access to find program requirements, even in the event of planned or unplanned downtime. Consider restricting dispensing access to only staff who have received training and have demonstrated competency in completing REMS activities. This limits the number of people who can handle these medications. One pharmacy reported that they have implemented hard stops to only allow authorized staff to process REMS medication orders.

Build ETASU directly into the EHR, pharmacy dispensing system, and/or clinical management software. Consult with information technology staff and/or the EHR or pharmacy computer system vendor to build fields into computer systems to capture REMS required information such as patient identification (ID) number, prescriber ID, authorization codes, and/or relevant laboratory data. Build in clinical decision support to notify practitioners that they are prescribing, dispensing, or administering medication with REMS program requirements and facilitate completion of any required REMS action. Ensure that reports may be easily generated for auditing purposes.

Limit prescribing to program-certified prescribers. Health systems and medical offices should only allow REMS-certified practitioners to prescribe medications that have this REMS program requirement. If possible, build in a prompt requiring a prescriber to enter their prescriber ID to continue placing the REMS medication order.

Educate staff and provide resources. Given the number of existing REMS programs, it is impractical for medical office and pharmacy staff to remember the requirements for each individual program. To optimize compliance, education should focus more on cues (e.g., flagging that a medication falls under the REMS category in the system) and knowing what resources (e.g., REMS policy, REMS resource binder) are available to comply with program requirements. Also consider the use of visual cues on pharmacy shelves to help staff identify REMS medications.

Identify barriers to obtaining REMS medications. Pharmacies should identify if REMS medications are available from their routine distributors and wholesalers, if the medication is a Limited Distribution Drug (LDD), or if there is a need to transfer the prescription to another pharmacy. Monitor usage and inventory levels to ensure enough medication is on hand. Prescribers should assess for barriers to patients obtaining the REMS medication (e.g., ensure prior authorization if applicable).

Develop a system to ensure the delivery of patient information. Institute protocols (e.g., automatic printout) to ensure mandatory patient information such as *Medication Guides* are distributed to the patient when a medication with a REMS program is dispensed or administered. Pharmacies call also investigate if their state regulations and pharmacy computer systems would enable the provision of patient education material, including *Medication Guides*, electronically (e.g., printing a QR code on the pharmacy label or receipt that links to the patient education material).

Ensure safe handling guidelines of hazardous medications. Several medications with REMS programs are considered hazardous and require certain handling procedures and/or may not be appropriate for certain patient or caregiver populations (e.g., pregnancy). Educate staff and patients on how to handle hazardous medications.

References

1) US Food and Drug Administration. Risk evaluation and mitigation strategies: REMS. Accessed June 26, 2023. www.ismp.org/ext/1089

2) Dabrowska A. FDA risk evaluation and mitigation strategies (REMS): Description and effect on generic drug development. ***Congressional Research Service***. March 16, 2018. Accessed June 26, 2023. www.ismp.org/ext/1090

3) Prescribers' Digital Reference (PDR). REMS summary of terms. Accessed February 6, 2023. www.ismp.org/ext/1178.

>SAFETY briefs

continued from page 2

(189 mg/mL) of inclisiran. The medication is intended to be administered by a healthcare practitioner as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of low-density lipoprotein cholesterol. Medical offices obtain Leqvio through either buy-and-bill (order the medication through a distributor) or from a specialty pharmacy.

We continue to communicate with the US Food and Drug Administration (FDA) about the broader issue of manufacturer prefilled syringes that do not have safety needle guards and will include this product in those discussions. We have notified Novartis, the manufacturer of Leqvio, about this latest report and recommended the addition of a needle safety guard to the prefilled syringe.

Preventing errors related to vaccine storage. Immunize.org (formerly known as the Immunization Action Coalition [IAC]) recently updated its document on preventing errors with vaccine storage and handling (*Don't Be Guilty of These Preventable Errors in Vaccine Storage and Handling!* www.ismp.org/ext/1152). The document gives advice on the types of refrigerators and freezers that are appropriate for storing vaccines. They note that vaccines and temperature monitoring devices should only be kept in the body of the refrigerator and, "not in the vegetable bins, on the floor, next to the walls, or in the door of the refrigerator, or near any cold air outlet from the freezer." Staff should not be allowed to store food and drinks in the vaccine refrigerator because the frequent opening of the refrigerator door to retrieve food items can adversely affect the internal temperature of the unit and potentially damage the vaccines.

Only store vaccines in designated refrigerators or freezers, where proper storage conditions can be regularly assessed and maintained. Consider conducting observational safety checks on vaccine storage after reviewing this latest update. See the Center for Disease Control and

continued on page 4 — SAFETY briefs >

Methotrexate injection dispensed without syringes and appropriate dosing information

When patients are prescribed injectable medications to self-administer at home, it is critical that they receive education from both the prescriber and pharmacist on proper injection technique, with clear verbal and written instructions on the dose volume to measure and administer, and are provided appropriate syringes, needles, and ancillary supplies (e.g., alcohol swabs) to administer the dose. Unfortunately, in a recent case reported by a patient, many of these steps did not occur when they started a new injectable medication.

A patient received a prescription for methotrexate injection for the first time. However, the prescriber and pharmacy provided administration instructions in terms of the mg dose rather than the mL dose volume. The pharmacy dispensed vials of methotrexate injection (50 mg/2 mL) labeled with the directions to "Inject 2.5 mg subcutaneously once weekly for 2 weeks then increase to 5 mg once weekly. May increase up to 10 mg once weekly." When the patient picked up the prescription, they were not offered counseling by the pharmacist. At home, the patient initially interpreted the instructions on the pharmacy label to mean that they should begin treatment by injecting 2.5 mL (or more than 60 mg) of methotrexate. The patient also realized the pharmacy did not provide syringes and needles to administer the methotrexate. The patient's roommate, who happened to be a pharmacy student, helped interpret the instructions, provided the correct initial dose volume of 0.1 mL (and each subsequent dose increase—0.2 mL [5 mg] and 0.4 mL [10 mg]), and informed the patient that they would need to return to the pharmacy to obtain 1 mL syringes to measure and administer the medication.

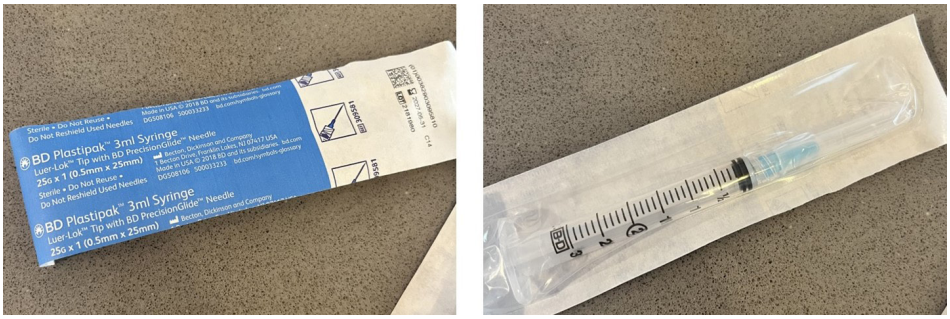

Figure 1. The pharmacy dispensed a 3 mL syringe with a 1-inch needle which is not appropriate to measure doses of 0.1, 0.2, or 0.4 mL, or for subcutaneous administration.

At the time of a subsequent refill of the methotrexate prescription, the pharmacy dispensed 3 mL syringes with 1-inch needles (**Figure 1**). While the syringe has markings for each tenth of an mL, it would be difficult for the patient to accurately measure their current 0.4 mL dose much less their earlier doses of 0.2 mL or 0.1 mL. Also, a 1-inch needle is appropriate for intramuscular, not subcutaneous injections. Subcutaneous injections require one-half to five-eighths inch long needles.

When prescribing and dispensing injectable medications for patients to self-administer, whether they come in a prefilled device (e.g., pen device) or a vial, it is critical that prescribers and pharmacists provide patient education and injection training. This includes how to use the device (e.g., syringe) to measure and administer the medication. Use the teach-back method to verify that the patient understands, and can demonstrate, how to properly prepare and administer the medication. Ensure the patient instructions printed on the pharmacy label include the dose in the unit of measure used for administration, which in the above case would be mL. Printing only the mg dose or even both the mg and mL dose on the pharmacy label can increase the risk of confusion for the patient. Dispense metric-only syringes, with needles of appropriate length and gauge for the route of administration, in volumes that most closely match the prescribed dose volume. Ensure the patient is provided with a sufficient quantity of syringes based on the frequency of injections and is educated on the appropriate single-use nature of syringes and needles (www.ismp.org/ext/1196) to avoid syringe re-use and potential contamination of multiple dose vials.

>SAFETY briefs continued from page 3

Prevention's (CDC) resource *Storage Best Practices for Refrigerated Vaccines* for more information (www.ismp.org/ext/1160).

Special Announcements

New! MSI workshop for community, mail order, and specialty pharmacy

Don't miss the opportunity to register for a unique, virtual ***ISMP Medication Safety Intensive (MSI)*** workshop designed for those working in **community, mail order, and specialty pharmacies**. Learn how to identify risks before they cause harm and how to use data for continuous improvement. This program will take place on two consecutive Fridays, **October 20 and 27, 2023**, from **7:30 am – 4:30 pm ET**. For more details about the program, please visit: www.ismp.org/node/75243.

Foundations in Medication Safety

ISMP's new online, interactive program offers **community pharmacies** a standardized, cost-effective way to ensure pharmacy staff have the baseline knowledge needed to promote safe medication use. For details, visit: www.ismp.org/node/76167.

Nominations open for CHEERS Awards

Nominations for this year's **CHEERS Awards** are now open and will be accepted through **August 6, 2023**. For more information, visit: www.ismp.org/node/123.

To subscribe: www.ismp.org/node/126

ISMP An ECRI Affiliate

ISMP Medication *Safety Alert!* Community/Ambulatory Care (ISSN 1550-6290)

Report medication and vaccine errors to ISMP: Please call 1-800-FAIL-SAF(E), or visit 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.