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

Incorporating REMS program requirements into systems and processes—Part II

Risk Evaluation and Mitigation Strategies (REMS) are required drug safety programs for certain medications that are designed to mitigate serious risks or errors. However, incorporating them into healthcare systems and processes is often complex and time-intensive. In **Part I** (www.ismp.org/node/87562), we discussed the number of different REMS programs and databases, the wide variety of requirements, a scarcity of implementation tools, and lack of organizational resources that have made it difficult for organizations and frontline practitioners to meet the various program requirements. In **Part II**, we describe how one health system, AdventHealth, was able to successfully operationalize REMS program requirements throughout the medication-use process.

AdventHealth has 51 hospitals in nine states with over 9,000 licensed beds. In 2016, the health system's medication safety team identified the need for a robust REMS infrastructure within the electronic health record (EHR). The team consulted with key stakeholders (e.g., prescribers, pharmacists, nurses) to gather feedback prior to obtaining committee approvals to initiate the project. They emphasized that this initiative would help the health system comply with the REMS program requirements, improve workflow for practitioners, and ultimately benefit patient safety. In 2017, they launched the workflow in the health system's EHR, which was Cerner at the time. In 2022, they transitioned to Epic and built a similar infrastructure into their new EHR system. Below is an overview of how AdventHealth implemented REMS safeguards across the inpatient medication-use system.

Developing an EHR Build Evaluation Tool and Identifying Medications

The medication safety team started by researching the various elements to assure safe use (ETASU) for the current US Food and Drug Administration (FDA)-approved REMS programs. Based on these requirements, the team created an EHR build evaluation tool for inpatient use to ensure they were adhering to and documenting each element within the REMS program (**Table 1** [page 4] provides an example of how the tool is used with ambrisentan [**LETAIRIS**]). Then they compared the list of medications with FDA-approved REMS programs and reconciled this with AdventHealth's existing formulary, to capture the appropriate medications for inclusion in the EHR.

Creating Policies and Procedures

The team updated an overarching policy that outlined the scope, purpose, and requirements, indicating how the health system and practitioners should manage REMS. A work instruction document was created that outlined the expectations for pharmacists to appropriately document the REMS medication requirements in the EHR. They also developed medication-specific standard operating procedures (SOP) based on nuances specific to the hospital set-up and workflow that could not be appropriately accommodated or captured in the EHR. For example, a clo**ZAP**ine SOP details how pharmacists can create an account associated with the hospital on the clo**ZAP**ine REMS website to retrieve a patient's REMS dispense authorization. In addition, there is a specific pulmonary arterial hypertension (PAH) service line that includes SOPs outlining processes related to oral and inhaled medications, including REMS enrollment requirements and pharmacy dispensing standards.

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Broken tamper-evident oral syringe cap. Many hospitals use plastic, tamper-evident caps for oral and parenteral syringes containing controlled substances. These may also be used by some 503B outsourcing companies for both controlled and non-controlled drugs. The syringe caps can be useful in making it easier to identify if tampering has occurred. But an organization reported that the stopper pin of an International Medical Industries (IMI) tamper-evident cap (**Figure 1**, page 2) made for Baxter Oral Dispensers broke off and remained within the tip of the syringe (**Figure 2**, page 2; **Figure 3**, page 3). Consequently, the plunger would not move when the nurse pressed it to administer the medication. When the nurse retrieved a second syringe, the same thing happened. They had to use a third syringe to administer the medication.

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IMPORTANT! Read and utilize the Acute Care Action Agenda

One of the most important ways to prevent medication errors is to learn about problems that have occurred in other organizations so that the information can be used to prevent similar problems at your practice site. To promote such a process, selected items from the **April – June 2023** issues of the ***ISMP Medication Safety Alert! Acute Care*** newsletter have been prepared for use by an interdisciplinary committee or with frontline staff to stimulate discussion and action to reduce the risk of medication errors. Each item includes a brief description of the medication safety problem, a few recommendations to reduce the risk of errors, and the issue number to locate additional information.

The **Action Agenda** is available for download as an Excel file (www.ismp.org/node/87900). **Continuing education** credit is available for nurses at: www.ismp.org/nursing-ce.

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Educating Practitioners

To ensure they were meeting the requirement to educate practitioners, the team established a formalized REMS education document (**Table 2**, page 5). This was used to guide the build of the educational modules in a learning management software for nurses and pharmacists to complete. For quality assurance, a report can be generated to confirm compliance. They also developed an email process for the Chief Medical Officer to notify physicians and other prescribers about medication-specific REMS education requirements. Realizing this process has the opportunity for improvement, they are currently exploring how to integrate this education requirement into their continuing medical education platform.

Updating the Formulary Process

After establishing the process for existing REMS medications, AdventHealth implemented a procedure for new formulary requests to indicate whether it is a REMS medication. When a REMS medication is approved for formulary addition, the post-pharmacy and therapeutics (P&T) workgroup utilizes a committee approval checklist to ensure all systems and processes have been taken into account (e.g., policy/procedure, education, appropriate storage, EHR medication builds, task and alert infrastructure, report generation). In addition, each site procuring the REMS medication designates a pharmacy lead as the authorized representative for program enrollment, as required.

Leveraging the EHR

The medication safety team worked with information technology, clinical documentation, and pharmacy teams to determine how the ETASU requirements could be built in a clear and accessible format to notify applicable practitioners (e.g., prescribers, pharmacists, nurses), and how to document the REMS-required information within the EHR. The team collaborated with end users to take into account their current workflow and incorporate requirements into the EHR infrastructure. This included utilizing a pharmacist-driven patient task list and documentation form to capture the specific ETASU; leveraging EHR functionality to only fire alerts for specific genders and age ranges (e.g., females of reproductive age); and embedding required laboratory tests into the prescriber alert to generate an order.

To ensure that all specific ETASU were met for each REMS medication, they built the following into the EHR:

- **Prescriber alerts:** When a REMS medication is ordered, an alert will notify the prescriber that this is a REMS medication. The alert is specific to the medication and includes a list of related requirements (e.g., patient and/or prescriber enrollment, laboratory tests). For example, the ambrisentan alert states "ambrisentan is an FDA REMS medication with the following requirements for female patients: prescriber enrollment (not required if continuation of home medication), patient enrollment, and a negative pregnancy test." In addition, the pregnancy laboratory result (date/time) will display, or if no result, the system will embed a pregnancy test order and a direct link to the prescriber section of the REMS website. The information in the prescriber alert can also be found in the order instructions, which can be viewed by all practitioners. If the medication does not require patient or prescriber enrollment or laboratory tests, then an alert will not fire, but the order instructions will specify the REMS medication status, along with any other specific information of which practitioners should be aware of (e.g., can dispense a maximum of 15 doses).

- **Pharmacist notification and documentation:** At AdventHealth, pharmacists are responsible for ensuring that patients and prescribers meet the ETASU requirements and that it is documented in the EHR. This electronic documentation can be easily retrieved for an internal or

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The pharmacy uses these caps after preparing a variety of oral liquid controlled substances in oral syringes. This was not the first time practitioners at this organization had experienced instances of cap tips snapping off in a similar fashion. The broken pin may prevent delivery of the medication, causing medication waste or a delay in care.

Figure 1. Tamper-evident caps by International Medical Industries (IMI) for use with Baxter oral syringes.

There is also a possibility that the broken pin may be dislodged from the syringe tip when the plunger is pushed, resulting in accidental ingestion of the broken pin when administered to the patient together with the oral solution, causing choking or asphyxiation.

Figure 2. A tamper-evident cap tip broke off and remained in the syringe tip, preventing a nurse from administering the medication from the oral syringe.

We reached out to IMI regarding concerns about delays in medication administration, or accidental ingestion or asphyxiation. IMI stated they have no reported instances of a broken pin becoming dislodged and no reports of patient harm due to this failure. Refer to the IMI product data sheet (www.ismp.org/ext/1176) to confirm the cap is compatible with the syringes used in your organization. Educate staff to pull the cap straight off the syringe, and to inspect the cap and the syringe tip opening after they remove a

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Coming soon: Applications for the **Judy Smetzer Just Culture Champion Scholarships** open **August 1, 2023**. Visit: www.ismp.org/node/30840.

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external audit. When a REMS medication requires documentation of patient and/or prescriber enrollment or laboratory tests, a clinical task is generated for the pharmacist to complete. The team created a template for pharmacists to document the required information as an intervention form. The template provides the specific requirements for each medication in a standard format so the pharmacist can verify if it is appropriate to dispense the medication. This may require the pharmacist to contact the REMS program to confirm prescriber and/or patient enrollment, obtain a REMS authorization number, or call the prescriber to order a laboratory test. Once they gather this information (e.g., laboratory test result), the pharmacist completes the intervention form and attests that all REMS requirements have been met for that patient. At this point, the medication order is ready for verification and dispensing. Of note, REMS contact centers are not available 24/7 for requirement confirmation. When patients are continued on their home REMS medication, and the contact center is unavailable, the pharmacist may verify the medication but leave the intervention open, so patient care is not delayed.

- **Nurse task for patient education:** Since nurses already had a designated area to document patient education in the EHR, the team advocated for a REMS education section. For any REMS medication with required patient education, a nurse education task was created that provides a link to the REMS website. The process allows the nurse to print the patient handout (e.g., medication guide), educate the patient, and complete the education documentation in the EHR prior to administering the first dose. This information is retrievable for auditing purposes.

Quality Assurance

As with any regulatory requirement, a proactive plan to demonstrate compliance is advised. For example, AdventHealth electronically captures documentation (e.g., EHR documentation by practitioners, completed education modules) for the various REMS elements. They also assign their pharmacy residents a REMS medication for completion of a medication use evaluation (MUE) each year. When a drug manufacturer or contracted third-party audits AdventHealth's REMS compliance, AdventHealth can readily retrieve and provide the requested REMS documentation.

Sustainment Plan

The medication safety team at AdventHealth has a proactive plan to capture REMS program changes (e.g., medication addition, deletion, modification) that includes biannual staff education, an annual policy review, and assigning a medication safety lead as the authorized representative to monitor REMS@FDA updates (to receive these updates via email, go to: www.ismp.org/ext/1174). Once the team identifies a change, they initiate the process described earlier, starting with completing or modifying the EHR medication build evaluation tool (**Table 1**, page 4). They also update the educational modules (**Table 2**, page 5) and reassign them to the practitioners to review the program changes. When onboarding new hires, these modules are integrated into the orientation program to ensure completion and compliance. To capture changes in pharmacy leadership, they also have a checklist incorporated into the orientation process to update the assigned REMS program authorized representative, if needed.

Next Steps and Additional Considerations

As mentioned, AdventHealth is comprised of 51 hospitals, and 130 clinics and other outpatient facilities across nine states. While the inpatient medication formulary has been the initial focus for the REMS medication builds and process, they plan to expand this project to the outpatient areas next. Another item for consideration is how organizations should handle non-formulary REMS medications. Currently, AdventHealth does not include these in the above REMS process. However, ideally, all REMS medications would be accounted for to ensure the same level of safety when

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tamper-evident cap and before administering the medication. Do not attempt to administer doses from an oral syringe if the cap appears damaged. Report any other issues to ISMP.

Figure 3. An intact tamper-evident syringe tip cap (top) and a broken one (bottom).

This is a different issue than what was reported in a 2019 article (www.ismp.org/node/11772), in which the plastic ring connected to the tamper-evident cap fell off and was not properly disposed of prior to administration. IMI told us that the oral tamper-evident cap was redesigned in 2021 such that there are no loose parts that separate from the tip cap.

Foiled again: Major Rugby barcode scanning issues. ISMP has received more than a dozen reports from healthcare practitioners who are unable to scan barcodes on unit dose packages of various over-the-counter medications from Major Pharmaceuticals and Rugby Laboratories (Major Rugby). Poor barcode readability when black ink is printed on reflective foil backing (**Figure 1**) is a long-standing issue. Several health systems reported a decrease in barcode scanning compliance from nearly 100% down to as low as 40%. One organization shared a list of the National Drug Codes (NDCs) on products that may be impacted (www.ismp.org/ext/1200).

Figure 1. Magnesium Oxide 400 mg tablets by Major Rugby with paper-backed foil (left) and the difficult-to-scan reflective foil backing (right).

The manufacturer notified the health system that the war in Ukraine has worsened an

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Table 1. EHR build evaluation tool for REMS medications using ambrisentan as an example.

REMS Name:	Ambrisentan (**LETAIRIS**)
Indication:	Pulmonary arterial hypertension
Why does it have a REMS requirement?	Risk of embryo-fetal toxicity
EHR Build needed? (Y/N)	Yes
What should be included in the order instructions?	Ambrisentan is an FDA REMS Medication for the risk of embryo-fetal toxicity with the following requirements for female patients: ▫ Provider enrollment (not required if continuation of home med) ▫ Patient enrollment ▫ Negative pregnancy test for reproductive, female patients ▫ Insert pregnancy lab result (date/time), If no result, embed pregnancy test order
Prescriber Alert? (Y/N)	Yes
Prescriber Alert Message:	Ambrisentan is an FDA REMS Medication with the following requirements: Provider enrollment (not required if continuation of home med), Patient enrollment, Negative pregnancy test (Insert pregnancy lab result [date/time]; If no result, embed pregnancy test order)
Pharmacist Intervention Task List? (Y/N)	Yes
Pharmacist Documentation needed? (Y/N)	Yes
Pharmacist Documentation template:	Ambrisentan (**LETAIRIS**) is a Risk Evaluation and Mitigation Strategy (REMS) medication. As part of the ordering process, it is required to meet certain requirements. 1) Is this a new start medication? Yes / No (continuation from home) 2) Patient enrollment in REMS program: Yes / No (contact the prescriber to get patient enrolled) / No (male patient -enrollment not required) 3) Enrollment number: ___ 4) Provider enrollment in REMS program: a) Yes (called REMS to verify) b) No (contact prescriber) c) N/A (continuation of home medication) d) N/A (male patient) 5) Is this patient a female of non-reproductive potential (FNRP)? a) Yes (pre-pubertal) b) Yes (post-menopausal) c) Yes (medical reasons for permanent irreversible infertility) d) Yes (consent form on file with REMS Program) e) No (patient is of reproductive potential) f) N/A (male patient) 6) Laboratory results in the last 30 days for a pregnancy test: (Insert pregnancy lab result [date/time]) 7) Is the patient pregnant? Must confirm a negative pregnancy test BEFORE verification of the medication. a) Yes; pregnancy test resulted positive. Do not verify the order and contact the prescriber (for new start orders) b) Yes; pregnancy test resulted positive. Do not verify the order and contact the prescriber and REMS program (for continuing orders) c) No; pregnancy test result negative (for new start orders) d) No; pregnancy test results negative or negative pregnancy test in last 30 days (for continuing orders) e) N/A (male patient or FNRP) 8) Are All REMS Requirements met? a) Yes; New start, dispense authorized b) Yes; Continuation from home; dispense authorized c) No; Requirements NOT met; dispense NOT authorized; Do NOT verify order and contact the prescriber
Nurse Education Task? (Y/N)	Yes
Medication Guide link for education task:	https://www.accessdata.fda.gov/drugsatfda_docs/rems/Ambrisentan_Shared_System_2021_06_08_Guide_for_Female_Patients.pdf
Laboratory order needed? (Y/N)	Yes
Laboratory order:	Pregnancy, urine last 30 days
Removal from REMS? (Y/N & Date)	No
EHR elements removed? (Y/N & date)	No

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these medications are prescribed, procured, and administered. Similarly, organizations should consider how they will screen orders for patients to use REMS medications brought from home, to assess if the medication has requirements that must be acted upon.

Conclusion

AdventHealth has made an upfront investment by operationalizing the REMS program requirements into various systems and processes including formulary management, EHR builds, policies/procedures, and educational modules. Although additional steps are planned, the medication safety team feels this structure and level of reliability has made a difference for their health system, practitioners, and patients. We encourage organizations to learn from this model when implementing REMS program requirements in your systems and processes.

We thank Jaclyn Jeffries, PharmD, CPh, Executive Director, Safety; Stacy L. Carson, PharmD, BCPS, FISMP, Medication Safety Officer; and Heather Ellis, PharmD, Medication Safety Coordinator, for sharing a systematic review of their REMS program processes and procedures, as well as helping to write this article. Email ISMP (ispinfo@ismp.org) with questions for AdventHealth.

Table 2. Example of the hospital's REMS education document template.

Generic (Brand) Name	ambrisentan (**LETAIRIS**)
Dosage Form	Tablet
REMS Purpose	Mitigate risks of embryo-fetal toxicity
Last Update	June 8, 2021
REMS Elements to Assure Safe Use (ETASU)	▫ Prescriber to be registered for all new start patients ▫ Dispensing pharmacy is registered by an authorized representative ▫ Staff involved in dispensing must complete education ▫ Verify the female patient is under the care of a certified prescriber and that she is or will be enrolled into the REMS program prior to discharge ▫ Confirmation of negative pregnancy test ▫ Counsel patient on the risk of embryo-fetal toxicity ▫ Do NOT distribute, transfer, loan, or sell REMS drug except to certified dispensers
Recent Updates	**Prescriber:** No recent updates, refer to Guidance Document (in Notes section) for full information. **Nurse:** No recent updates, refer to Guidance Document (in Notes section) for full information. **Pharmacist:** No recent updates, refer to Guidance Document (in Notes section) for full information.
Notes	▫ Formulary medication ▫ Shared system REMS ▫ Link to Ambrisentan REMS Guidance Document

Special Announcements

ISMP confused drug name list updated

We recently updated our ***List of Confused Drug Names***. It is one of the most comprehensive references available! Organizations are urged to use the list to determine which medications require special safeguards to reduce the risk of errors. Find the list at: www.ismp.org/node/102.

Last call for CHEERS Awards nominations

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

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industry-wide supply issue with foil. As a result of the foil shortage, they made a short-term change to the type of foil backing they use. Major Rugby is expediting a return to the original paper-backed foil and plans to have them available for distribution. In the meantime, consider repackaging or relabeling these products with readable barcodes.

Update on leaking ports with ExactaMix 2400 compounder. On June 28, 2023, Baxter released an urgent medical device correction follow-up letter (www.ismp.org/ext/1201), addressing the July 2022 communication regarding the potential for leaking **EXACTAMIX** 2400 valve set ports. We shared information about this issue in a previous publication (www.ismp.org/node/39585). In this follow-up letter, Baxter states that it has implemented actions to correct the potential for leaking valves in the ExactaMix 2400 valve sets, including the deployment of new molding equipment and an improved assembly process. Baxter also states that customers may return to using all 24 ports on their compounders when using the newly manufactured ExactaMix 2400 valve sets (product code H938724, lot numbers 60459942 and above). If your organization is still using or still receiving valve sets with lot numbers below 60459942, to prevent a valve set shortage, Baxter recommends continuing to follow the configuration instructions that omit the use of ports 1 to 4 until your supplies are depleted. Please review the updated ECRI Hazard Report (www.ismp.org/ext/1199) for additional information.

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