

Pharmacists, Deluged With Requirements, Pressure FDA to Standardize REMS Programs

Stephen Barlas



Mr. Barlas is a freelance writer in Washington, D.C., who covers issues inside the Beltway. Send ideas for topics and your comments to sbarlas@verizon.net.

The FDA plans to make a multifaceted effort to simplify life for pharmacists, physicians, and patients who have to navigate the often-confusing world of Risk Evaluation and Mitigation Strategy (REMS) programs. Drug manufacturers are required to develop a REMS under the FDA's guidance for new drugs that pose significant risks. REMS programs come in different flavors; they can be as long as 100 pages and are crammed with various communication, intervention, registration, or verification elements, some of which pharmacists must satisfy. In some instances, pharmacies have to be specially enrolled to dispense a drug with a REMS.

A REMS is rarely a carbon copy of any other one. In some cases, a drug must be distributed by a specialty pharmacy. The most decorated pharmacist working in a blue ribbon, non-specialty pharmacy can be denied access to a REMS drug for reasons only the manufacturer knows and does not have to disclose. A patient might be required to undergo weekly or monthly laboratory testing; sometimes the testing can be done at home. A pharmacy, if it is lucky enough to be accepted by a REMS program, must be aware of each "i" that needs to be dotted and each "t" that needs to be crossed.

Christopher J. Topoleski, Director of Federal Regulatory Affairs, American Society of Health-System Pharmacists (ASHP), says, "The Society is concerned that current REMS programs are negatively affecting the already limited time that pharmacists have to care for and ensure the safety of their patients."

Not only are REMS programs time-consuming for pharmacists; a REMS can also be an impediment to hospitals that

receive certain drugs for inpatient use. This is because manufacturers prefer to distribute those drugs only to specialty outpatient retail pharmacies, which ostensibly have the expertise needed to handle the drugs in a way that reduces risks to patients and liability potential to the manufacturers.

Katie Stabi, PharmD, BCPS, Drug Information Pharmacist (REMS) at Cleveland Clinic, is in charge of coordinating REMS drug access for the medical center's 10 regional hospitals and multiple outpatient pharmacies. When enrollment into a REMS program is required, the director of pharmacy or the P&T committee chairman signs on the dotted line. After the inpatient pharmacy is enrolled, all of its pharmacists may handle REMS medications. The pharmacists are subject to verification and other requirements that, again, may vary from drug to drug. Each pharmacist must receive training and instruction, if required, regarding the drug's idiosyncratic effects.

The FDA requires a REMS program for about 70 drugs. In six of these cases, the REMS covers an entire class of drugs ("shared" REMS). About half of currently approved REMS programs include Elements to Assure Safe Use (ETASU). These especially prickly demands require significant outlays of time on the part of physicians and pharmacists. A list of REMS drugs is available at the FDA's website.¹

Among the reasons that the FDA demanded a REMS program for Celgene's lenalidomide (Revlimid), for example, was an association with a significantly increased risk of deep vein thrombosis and pulmonary embolism in multiple myeloma patients who had received this drug plus dexamethasone. There was also a risk for embryofetal toxicity. The REMS produced by Celgene for lenalidomide is 100 pages long. Paul Sheehan, head of U.S. REMS for Celgene, declined to discuss this REMS.

Sometimes inpatient and hospital outpatient pharmacies are precluded from enrolling in a REMS because the drug's

distribution is restricted to specialty pharmacies. Dr. Stabi says:

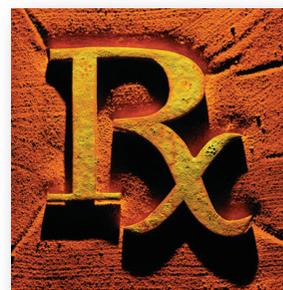
We have one pharmacy that dispenses high-cost, highly specialized medicines for diseases such as cancer. Although this pharmacy is not designated as a specialty pharmacy, the pharmacists are able to handle the complex requirements of REMS drugs. Yet medications that have similar REMS programs, such as Revlimid, Thalomid, Pomolyst, are not all available to that pharmacy due to the restricted distribution of those REMS programs.

Even when an inpatient pharmacy is theoretically qualified to enroll in a REMS program, it might not be able to do so. Several REMS programs are similar to the iPledge Shared System, the shared REMS for the acne drug isotretinoin (Accutane, Roche), for which a prescription window and a survey are required. The iPledge Web site states that hospital pharmacies must follow all of the requirements of the iPledge program and may not process partial isotretinoin prescriptions or break blister packs. Dr. Stabi explains:

This process is burdensome for inpatient dispensing, since orders, not 30-day prescriptions, are usually written, and individual doses are dispensed daily. While it is our hospital policy to supply patient medications to ensure safety and appropriate storage, we are not able to do this with programs that have prescription windows and similar burdensome requirements.

Instead, Cleveland Clinic has a process in place for patients to provide their own medication. This can be difficult when a patient forgets the drug at home or the prescriber caring for the patient is not familiar with the REMS program requirements.

In some instances, patients must be tested in order to receive a drug with a REMS, either at a laboratory or perhaps at home, before they can receive a refill. Patients have arrived at a Cleveland Clinic outpatient pharmacy that was not eligible to dispense the drug.



The inpatient pharmacy might have the drug, because drug reimbursement is bundled into Diagnosis-Related Group (DRG) payments—meaning that hospitals have easier access to REMS drugs on an inpatient basis. In this situation, Dr. Stabi might call the manufacturer, only to be told that she may not send the drug across the street to the outpatient pharmacy unless she admits the patient to the hospital for laboratory testing. A hospital admission, of course, leads to higher costs for patients.

This scenario helps to explain why health care systems want the FDA to permit them to enroll in a REMS, so that all hospital inpatient and outpatient pharmacies are under one corporate roof and can dispense a drug under one enrollment.

“If a single certification were in place that enables all pharmacies in an integrated system to dispense the drug, this patient would have immediate access to the medication after verification of REMS requirements and could prevent possible hospital admissions to receive maintenance therapy,” Dr. Stabi says.

The FDA has made some efforts to ease the burdens on physicians, pharmacists, and patients by developing shared REMS. For instance, the agency put in place the single, shared REMS for isotretinoin in October 2010. Although this made life easier for physicians and pharmacists, the REMS program is still in need of reform, according to pharmacists and others—hence the push for a single health care system enrollment.

C. Douglas Monroe, RPh, MS, is the Pharmacist Project Manager for Biotechnology, Emerging Pharmaceutical Technology, and Specialty Pharmacy, Drug Information Services, at Kaiser Permanente. He wants the FDA to allow health care system pharmacies to certify a “representative pharmacist” and to require procedures for training dispensing pharmacists and for ensuring REMS compliance.

He says, “Ensuring that every pharmacist is trained and certified can be time-consuming and introduces new opportunities to delay patient access to drugs. With multiple drugs with REMS, burdens are multiplied.”

The American Pharmaceutical Association (APhA) opposes the idea of a REMS certification for a single health system. Thomas E. Menighan, BS Pharm, MBA, Executive Vice President and Chief Execu-

tive Officer of the APhA, says it should not be too burdensome to spend a few minutes learning the nuances of a REMS program for pharmacists who dispense and teach patients safe use. He commented:

Delegating this responsibility to the system or to the pharmacist in charge increases the risk that a knowledge gap will lead to REMS failure. If health system-level certifications became the norm, it might be difficult to ensure that all providers have the requisite knowledge and resources to safely and effectively provide REMS medications to patients.

The FDA is considering changes to its REMS requirements, in part because of the FDA Safety and Innovation Act of 2012 (FDASIA) and in part because of criticism in a report, published in February 2013, from the Office of Inspector General (OIG) at the Department of Health and Human Services (DHHS).²

The FDA was already aware of some of the shortcomings of its REMS program and was moving to address them. In 2011, the agency created the REMS Integration Initiative, designed to evaluate and improve its implementation of REMS authorities.³ However, Congress pressed the agency to do more to conform to the language of the FDASIA. The FDA, for its part, promised to hold one or more public meetings to explore strategies to standardize REMS and to reduce the burden of implementing REMS on practitioners, patients, and others in various health care settings. A meeting held last summer produced all sorts of complaints and suggestions from various pharmacy industry groups, among others.

“The lack of standardization results in large amounts of duplication within health care systems,” says Christopher Topoleski. “Further, the lack of centralized or standardized methods for accomplishing the elements to assure safe use collectively for all REMS is a burden.”

To satisfy congressional requirements stemming from FDASIA, the FDA will be issuing a report of its findings regarding standardizing REMS. The report will identify priority projects in four areas (pharmacy systems, prescriber education, providing benefit–risk information to patients, and practice settings).

The FDA also promised to issue guidance on ways to assess REMS programs.

Specifically, it would devise methods to determine whether a REMS with ETASU is commensurate with the serious risk listed in the drug’s labeling (and considering the observed risk, not unduly burdensome on patient access to the drug).

One pilot project the pharmacy industry would like to see involves standardizing Structured Product Labeling (SPL) of REMS. SPL is a document-markup standard approved by Health Level Seven International (HL7) and adopted by the FDA as a mechanism for exchanging product and facility information.

Gerald K. McEvoy, PharmD, Lead of the National Council for Prescription Drug Programs SPL REMS Requirements Task Group, is heading an effort to wrestle REMS data into the optimal electronic format so that it can be included in the SPL model. His day job is Assistant Vice President of Drug Information at the ASHP. The ASHP has been working closely with National Council for Prescription Drug Programs, the FDA, and a broad base of stakeholders to help define how SPL can best be used to support such REMS standardization efforts. A number of roadblocks are in the way, however. For example, there is no highly structured submission requirement for an electronic REMS. Electronic versions of REMS are Portable Document Format (PDF) files and word-processing documents.

Fitting REMS compliance smoothly into an electronic prescribing format would make life considerably easier for pharmacists; so would developing a standardized five- or 10-page REMS form. Ideally, the upcoming FDA pilot projects will be moving toward those objectives.

REFERENCES

1. FDA. *Approved Risk Evaluation and Mitigation Strategies (REMS)*. Update, October 15, 2013. Available at: www.fda.gov/drugs/drugsafety/postmarketdrug-safetyinformationforpatientsandproviders/ucm111350.htm. Accessed October 30, 2013.
2. Office of Inspector General. *FDA Lacks Comprehensive Data to Determine Whether Risk Evaluation and Mitigation Strategies Improve Drug Safety*. Report (OEI-04-11-00510), February 12, 2013. Available at: <https://oig.hhs.gov/oei/reports/oei-04-11-00510.asp>. Accessed October 30, 2013.
3. FDA. *REMS Integration Initiative*. May 29, 2013. Available at: www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUser-Fee/ucm350852.htm. Accessed October 30, 2013. ■