

Smoothing the Path to Drug Safety

Virginia, Virginia Commonwealth University, in a recent Medical News article on the planned class-wide opioid REMS.

Kaiser Permanente filed a Citizen's Petition on December 22, 2009, asking FDA to seek public input from patients or healthcare providers before implementing REMS. Kaiser is concerned that REMS with ETASUs may increase burden on healthcare providers and drive up costs, resulting in avoidance of essential drug use.

REMS and unintended consequences

FDA explicitly states in its guidance document (August 2009) that the agency seeks to avoid what they term "unintended consequences" of REMS programs in their quest for improving drug safety. Nevertheless, FDA is not involved in designing the details of REMS processes—this responsibility falls on the pharmaceutical industry and biotech manufacturers who must ensure execution of their REMS while trying to minimize the unintentional impact on stakeholders and access. Also, FDA does not usually have any direct regulatory interaction over many of the stakeholders (e.g., pharmacies) that are directly affected by REMS programs.

Stakeholders have identified some key, unintended outcomes resulting from REMS:

- "Squeezing" or restricting drug use with a REMS for certain products results in expanded prescribing of alternate, less desirable agents—also known as the "balloon effect."
- Impeding patient access to medications by adding additional steps or limited distribution. For example, a pharmacy may need to verify that a prescriber is registered in a REMS database thus increasing the number of patients who do not initiate or lapse on therapy.
- Increased, uncompensated costs to healthcare providers in meeting REMS requirements, such as added paperwork or additional counseling.
- Altering the efficient existing workflow with REMS requirements and imposing additional reporting requirements, or recordkeeping for audit purposes.

Easing the pain

The goal of pharmaceutical manufacturers of REMS programs should be to preserve safety goals without creating obstacles or excess work for healthcare providers. In order to accomplish this goal, manufacturers should view REMS from the user's viewpoint—what is the usual flow of practice activities? Where, when, and how are decisions about therapy made? How and when do patients access medications? What processes of automation and technology are used and could be leveraged by a REMS system? The order and types of processes employed may differ in various healthcare settings.

Stakeholder workflow is paramount

Stakeholder workflow is not a factor independent of the actual number or type of additional restrictions or steps required by a REMS—rather, it is a measure of how much the REMS requirements force deviation from the usual routine and systems that the healthcare provider typically uses. For example, a REMS program that requires a pharmacist to access Web-based systems, as opposed to their usual pharmacy dispensing system has a negative impact on stakeholder workflow. In other cases, a physician who does not use electronic medical records (EMR) for patients at all may paradoxically find a paper-based system is less intrusive, since it integrates into existing workflow. For the same reasons, healthcare providers find that there are coordination and tracking challenges if REMS programs require recordkeeping or tracking of patients outside of their usual processes. Therefore, manufacturers should consider the various steps that occur in a REMS from the decision to prescribe a medication to the point-of-dispensing and examine the potential obstacles and solutions for each. A brief analysis follows.

1.

The pre-prescribing decision

In some REMS programs, pharmaceutical and biotech manufacturers must implement educational programs, which provide prescribing physicians with information on the risks of the product prior to ever starting any

patients on therapy. These educational interventions often have a knowledge test that a potential prescriber must periodically complete and pass prior to be a verified and eligible prescriber. This educational process has happened for decades but never before has FDA and, by extension, the manufacturer been as prescriptive as to how, when, and in what exact format the education must take place. The workflow of pre-prescribing has been disrupted, though in this case, it is likely the intention of FDA to have risk information accepted and attested to by providers prior to prescribing.

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In general, pre-prescribing education is a one-time event in a REMS program; so healthcare providers find this to be one of the less cumbersome elements. Nevertheless, there are ways of improving the interaction:

- Ensure a smooth, high-quality process with clear, transparent communication around the expectations, feedback, steps in the process as well multiple options for providers.
- Technology may be useful in helping prescribers keep track of their enrollment status. Since programs require periodic re-certification over time and prescribers will enroll in multiple programs, the technological solutions that allow practices to track of multiple registrations will be helpful.

2.

Therapy initiation

Once the pre-prescribing stages of REMS are complete, a provider begins selecting patients based on the balance of potential benefit and risks. With REMS programs, there are new steps required at therapy initiation to ensure that patients have adequate information about the risks of the product. These educational discussions have been ongoing between physicians and other clinical providers for years but now FDA has once again become prescriptive and focused on consistent, documented delivery of risk messages.

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- The concept of “certified counseling” is something that is being explored with pharmaceutical manufacturers. Clearly, the prescriber must be involved in risk conversations, but may be able to permit staff that has been trained on the specific REMS elements to assist. These conversations may be possible by phone. While FDA has, in our experience, not always been supportive of interactive voice response (IVR) systems, we believe that a well-designed system can attain safety goals and remove some of the more repetitive elements of risk communication with patients. One must also recognize that while the written information in medication guides is relatively easy to develop, REMS programs often require that the prescriber ensures that the patient reviews and attests to understanding its content – often a more involved process than it sounds. Focusing on ensuring patient comprehension is key.

3.

Patient therapy maintenance and follow-up

Providers must now work with their patients to comply with ETASUs that are required on an ongoing basis. Various data may need to be provided to the manufacturers, or specific diagnostic and therapeutic interventions completed based on evaluations of patients’ status, examination, and test results. Patients may need to comply with periodic clinical counseling calls to understand and detect risk signals in the population and provide opportunities for early intervention.

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More than any other area, integration with existing healthcare-provider systems offers an opportunity to make REMS programs easier in patient therapy and follow-up:

- Physicians—Many community practices have yet to adopt EMR, e-prescribing, or electronic connectivity for laboratory and other test results. However, EMR has the potential to allow automation of many

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ETASUs, such as prescriber or patient enrollments. The marketplace will await REMS specific applications that are embedded in EMRs.

- **Pharmacies**—Unlike physicians, all pharmacies are connected and routinely use electronic systems to manage their own workflow, patient records, and connectivity with payers. Furthermore, multiple pharmacies, whatever their location, are linked to payers through nationwide switch systems. As a result, during dispensing of prescriptions, it is relatively easy and non-disruptive to introduce REMS controls that allow pharmacists to obtain online verification of the eligibility of prescribers, which is fully integrated into routine pharmacist workflow. REMS providers, including McKesson Relay Health, are developing this approach for high-volume, retail-pharmacy dispensed drugs.
- **Wholesalers**—Electronic exchange of information has been used for a variety of purposes in the wholesaling industry. Verification of REMS requirements (like registration status of a clinic, hospital, or physician office) can occur electronically, limiting the impact on the typical workflow for a distributor.

REMS usability is a key element to success

As REMS become more common in the near future, pharmaceutical and biotechnology companies must invest in developing internal expertise in the forecasting for REMS, design of REMS, program management, and change processes. Unfortunately, the penalty is high for pharmaceutical companies that do not take this approach. The biggest fear that pharmaceutical manufacturers have regarding REMS programs is the potential to limit or shrink their franchise. A REMS program that neglects to consider usability in the hands of healthcare providers and stakeholders incurs this risk.

Other trends that pharmaceutical manufacturers should consider are:

- Healthcare providers and patients want the FDA to develop a more transparent process to disseminate the data and lessons from existing REMS programs. Their rationale is that FDA needs to give more timely feedback on success and failures, in order to react and rapidly process iterative improvements, or even eliminate certain REMS programs or components if no incremental benefit is observed.
- Pharmaceutical manufacturers need to go wide and deep to obtain an in-depth perspective from providers that will be affected. The challenge for industry is to balance the feedback from providers with the need to create a program that FDA will approve. While pharmaceutical manufacturers are accountable to FDA, they must constantly focus on usability to ensure success. **PC**



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