BRIEF COMMUNICATION

Extended-release/long-acting opioid REMS may fill the need for prescribers' appropriate use education

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ABSTRACT

The Food and Drug Administration (FDA) is requiring manufacturers of long-acting and extended-release opioids to have a class-wide Risk Evaluation and Mitigation Strategy (REMS). The comprehensive risk management plan will include training for prescribers on the appropriate and safe use of these pain medications. The letter dated April 19, 2011 from FDA to manufacturers outlining the REMS requirements describes voluntary training that should be certified education "where practicable." The current report includes data from a recent comprehensive study of healthcare professionals and patients and highlights key insights that can guide the development of the opioid REMS training.

INTRODUCTION

Risk Evaluation and Mitigation Strategies (REMS) are Food and Drug Administration (FDA)-mandated risk management programs for drug manufacturers. There are very specific obligations that companies must fulfill on a strict timeline to avoid monetary penalties and civil liability of responsible people. Since the enactment of REMS requirements in March 2009, the pharmaceutical industry, healthcare professionals, and FDA have been on a steep learning curve as we collectively figure out the best way to implement REMS.

More than 200 REMS have been approved since the initiation of the REMS requirements in 2009. Most approved REMS required medication guides only, which are part of drug labeling, and contain risk information in patient-friendly language. Recently, in February 2010, the FDA issued new guidance limiting the use of only these less burdensome, medication guide REMS. Consequently, more than 80 REMS have been "released" as the FDA viewpoints on what should constitute REMS evolve. It seems reasonable to presume that future REMS will largely be REMS with more involved elements to assure safe use (ETASU). ETASU include one or more of the following: prescriber training/certification; certification of drug dispensers; drug dispensing limited to tightly controlled settings; drug dispensed only with documentation of safe use conditions; monitoring of patients; or patients enrolled in a registry.

One REMS has cast a long shadow over the industry and the healthcare system; the class-wide extended-release/long-acting (ER/LA) opioid REMS. In February 2009, FDA notified the manufacturers of these products that a REMS would be required and the obligations shared by all companies.[1] The initial goal of the ER/LA REMS was "to ensure that the benefits of the drugs continue to outweigh the risks through: proper patient selection; minimizing the risk of overdose, both accidental and intentional; minimize the risk of abuse; to ensure that prescribers, dispensers, and patients are aware of and understand the risks and appropriate use of these products."[1] This began a process that involved 2 years of communication between industry, FDA, bodies that accredit medical education, and stakeholders, including healthcare providers (HCPs), health systems, professional societies, and patients. During this time, all parties gained a deep appreciation of the complexity of enacting a risk management program that would impact approximately

four million patients and approximately 680,000 Drug Enforcement Administration-registered prescribers. Much consternation was expressed over the possibility of inadvertently denying patient's access to pain-appropriate pain medications in our efforts to minimize the risks of ER/LA opioids.

On April 19, 2011, the FDA sent official letters of notification of a REMS requirement to the ER/LA opioid manufacturers.[2] The letter was sent to 18 companies, and it encompasses 12 branded and 23 generic products.[3] The letter delineated that the new safety information that prompted the REMS requirement is "substantial numbers of postmarketing reports of abuse, misuse, addiction, and overdose resulting in fatalities associated with extended-release and/or long-acting opioid drugs."[2] The REMS is to "ensure that the benefits of the drug continue to outweigh the risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate prescribing, abuse, and misuse." The REMS will include medication guides, ETASU, and assessments; the ETASU consists of voluntary prescriber training. The FDA has requested in the postapproval letter that the training should be conducted by accredited, continuing education providers "to the extent practicable." Based on stakeholder feedback, continuing education credits are perceived as an important incentive to get practitioners to participate in voluntary training.

There are very specific guidelines around industry's involvement in continuing education.[4] To explore the necessity of this incentive for prescriber training on the appropriate use and risks of ER/LA opioids, a study was conducted to evaluate the understanding of HCPs about REMS, perception of challenges around opioid prescribing, and their predictions of what the impact of this REMS will have on their practice patterns.

METHODS

The study was conducted from March 2011 to May 2011. A survey was fielded to US-based HCPs: primary care physicians (PCPs), pain specialists (PS), and pharmacists (PHs). In addition, a nested patient survey was conducted.

The protocol and survey instruments were reviewed by Western Institutional Review Board (WIRB; Olympia, WA) prior to study implementation. Full methodological information can be found in the article by Salinas et al.[5]

RESULTS

The survey captured data from 193 PCPs, 147 PS, and 150 PHs. REMS awareness was generally high with 65 percent of PCPs, 86 percent of PS, and 67 percent of PH being either very or somewhat familiar with the FDA's proposed REMS for ER/LA opioids. The remaining HCPs were not familiar with the REMS. When asked about what impact the REMS might have on their practice or patients, there was ambivalence around what the impact might be (Figure 1).

Most patients believe their physician is the most important resource for them in terms of managing their pain (Table 1). This does not obviate other sources of information as being important to patients such as pharmacists, nurse practitioners, physician assistants, the Internet, educational materials, and others.

When asked where they got information on the safe and effective use of opioids over the past 2 years, HCPs identified certified educational programs as their primary source of information (Figure 2). Required REMS training programs and voluntary REMS training programs were much less frequent sources of information.

DISCUSSION

The treatment of chronic pain patients presents a challenge for PCPs. The proper use of opioids for patients requires PCPs to balance the need for appropriate pain management with the fear of overtreatment or possibly contributing to the problem of misuse and abuse. While the inclusion of a PS in the treatment plan for patients could ameliorate the apprehension of PCPs, patient appointments may be difficult to get or these specialists may be too distant to be useful to patients. Consequently, there is a need for PCPs to be up-to-date and comfortable with their knowledge of the appropriate use of pain medications, particularly opioids.

Patients rely on PCPs to be knowledgeable about treating their pain. To a lesser degree, patients rely on pharmacists, nurse practitioners, and physicians' assistants to fill this role. Although many patients turn to the Internet for information, these tools may be less informative for the patient trying to understanding their personal risk/benefit than a discussion with their personal physician. REMS offer the promise of bringing ER/LA opioid appropriate prescribing and safe use information to physicians. The use of a class-wide

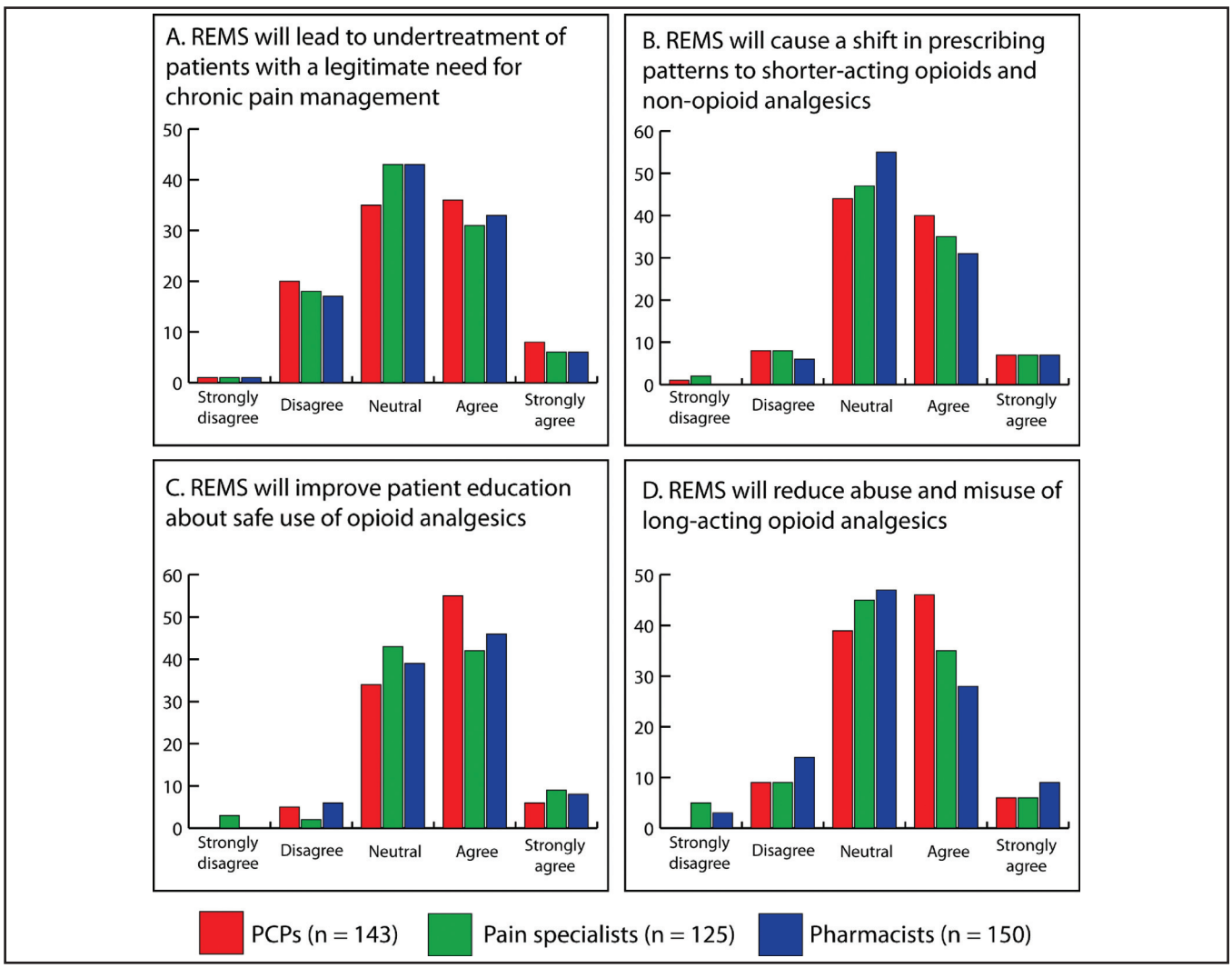

Figure 1. Perception of REMS impact on practice. A large percentage of clinicians who are aware of the FDA's proposed opioid REMS policies are ambivalent about the impact.

REMS requirement by the FDA to bring together 18 or more companies to create an educational platform for ER/LA opioids is very ambitious. The ETASU physician training component of the REMS is a key element to this approach. This study offers important insights into what physicians identify as the potential impact of REMS on their practices and how they plan to participate in opioid risk education. Currently, there are many existing programs available to physicians that address appropriate use of opioids. Some of them are product-specific training programs (Exalgo™), Nucynta® ER, Oxycontin®, and Butrans®), some are required REMS certification programs (Onsolis™), and some are certified educational programs from accredited medical education providers. Importantly, for physicians and pharmacists, continuing education/continuing medical education (CE/CME) represents the largest portion of educational activities they participate in, potentially due to the development of content by parties independent of the manufacturer. CE/CME is required in most of the 39 jurisdictions of the Federation of State Licensing Boards and also for maintenance of certification for HCPs.

Despite several public meetings and press releases around government action on the opioid issues since the announcement of the class-wide opioid REMS, a surprisingly large minority of PCPs are neither aware of the REMS nor they have a clear understanding what the impact of REMS will be on their practice. Although there is clearly an educational gap for PCPs with regard to the appropriate and safe use of opioids,[5] how to fill that gap with REMS in the most effective manner is yet to be

Table 1. Importance of pain treatment information sources for patients		
Please rate the importance of the following resources for guidance on how to manage your pain:	**Managed by PCPs**	**Managed by pain specialists**
Primary care doctor	n = 90	n = 67
Not important (1)	12 percent	10 percent
(2)	3 percent	5 percent
(3)	17 percent	12 percent
(4)	36 percent	54 percent
Very important (5)	32 percent	19 percent
Doctor specializing in pain management	n = 48	n = 69
Not important (1)	6 percent	0 percent
(2)	19 percent	3 percent
(3)	2 percent	1 percent
(4)	13 percent	25 percent
Very important (5)	13 percent	71 percent
Nurse practitioner	n = 47	n = 64
Not important (1)	13 percent	0 percent
(2)	8 percent	6 percent
(3)	12 percent	12 percent
(4)	12 percent	42 percent
Very important (5)	7 percent	33 percent
Pharmacist	n = 78	n = 58
Not important (1)	14 percent	4 percent
(2)	19 percent	16 percent
(3)	19 percent	26 percent
(4)	22 percent	26 percent
Very important (5)	13 percent	12 percent
Psychologist/mental health professional	n = 49	n = 40
Not important (1)	11 percent	17 percent
(2)	16 percent	12 percent
(3)	12 percent	4 percent
(4)	11 percent	20 percent
Very important (5)	4 percent	4 percent
Online websites	n = 72	n = 59
Not important (1)	7 percent	9 percent
(2)	24 percent	6 percent
(3)	28 percent	29 percent
(4)	14 percent	30 percent
Very important (5)	7 percent	12 percent

(continued)

Table 1. Importance of pain treatment information sources for patients (continued)		
Please rate the importance of the following resources for guidance on how to manage your pain:	**Managed by PCPs**	**Managed by pain specialists**
Patient education materials from doctor	n = 76	n = 64
Not important (1)	3 percent	3 percent
(2)	20 percent	7 percent
(3)	32 percent	29 percent
(4)	20 percent	39 percent
Very important (5)	9 percent	15 percent
Pain management hotline	n = 67	n = 37
Not important (1)	23 percent	13 percent
(2)	19 percent	13 percent
(3)	13 percent	1 percent
(4)	12 percent	16 percent
Very important (5)	7 percent	10 percent

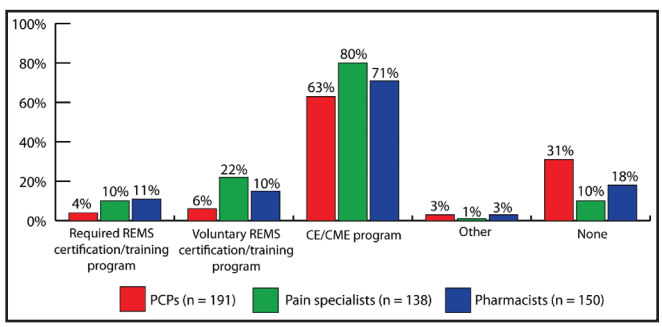

Figure 2. HCP sources of opioid education. Survey respondents selected the type of educational programs on safe and effective use of opioids in which they have participated in the past 2 years. Required REMS training includes Onsolis™. Voluntary REMS training includes OxyContin®, Butrans® Nucynta® ER, and Exalgo™.

determined. This study suggests that CE/CME is likely to be a preferred method of opioid education for all prescribers and pharmacists. Importantly, patients are relying on all the three groups of HCPs to be well informed and serve as a resource to them in their quest for the most effective and safest treatment for chronic pain.

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