Primary care physician opinion survey on FDA Opioid Risk Evaluation and Mitigation Strategies

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ABSTRACT

Introduction: In response to disturbing rises in prescription opioid abuse, the Food and Drug Administration (FDA) has proposed the implementation of aggressive Risk Evaluation and Mitigation Strategies (REMS) that will require prescribers to obtain mandatory education, provide mandatory patient education, register patients into registries, and so forth before prescribing certain opioids. The first opioid to be subject to the new REMS was the recently approved fentanyl buccal soluble film (Onsolis™). The FDA plans to extend mandatory REMS to other opioids, including all rapid-onset formulations and eventually all long-acting opioids, whether or not they already have FDA approval. To assess the likely impact of REMS on opioid prescribing, the authors conducted a survey of how REMS implementation might affect opioid prescribing.

Methods: After obtaining Institutional Review Board’s approval, a survey regarding opioid prescribing was sent via e-mail to 2,800 physician members of the Pennsylvania Academy of Family Physicians. Practicing family practice physicians were asked to respond to questions regarding their current opioid prescribing, and how various components of REMS might alter their future opioid prescribing.

Results: A total of 259 surveys were completed. Of the 259 physicians who responded, 87 percent reported themselves as being primary care practitioners; others identified themselves as specialists. Of all respondents, 96 percent currently prescribe opioids for acute pain, 77 percent for cancer pain, and 83 percent for chronic nonmalignant pain. The respondents were split from 52 percent to 48 percent in terms of being in an urban versus a rural practice setting. Forty-eight percent of all respondents reported their willingness to complete no more than 2 hours of training if it were available locally to be able to continue prescribing opioids. A similar percentage (50 percent) also said that they would encourage patient compliance with education and register their patients on a 6-month basis. However, the following percent of respondents reported that they would discontinue prescribing an opioid product if required to comply with the following REMS requirement: obtain 4-8 hours of training, followed by 2 hours of pain-related continuing medical education every 2 years (13.4 percent); complete mandatory patient education (12.2 percent); document ongoing monitoring of therapy including efficacy, safety, and monitoring for aberrant drug-related behavior (10.4 percent); or register each patient in a patient registry, and have the patient re-registered every 6 months (18.3 percent).

Conclusions: The results suggest that 50 percent of the responding physicians would be willing to comply with the mandatory education component of REMS, including the requirement to provide education to patients. For some REMS components, willingness to continue prescribing despite the restriction was higher (up to 90 percent). However, this leaves a substantial proportion of physicians who would not be willing to prescribe opioids controlled by the new REMS, which could have the unintended effect of decreasing access to these medications for legitimate medical purposes.
INTRODUCTION

The incidence of prescription opioid abuse in the United States has grown dramatically in the last 20 years. This is mirrored by an overall increase in the use of opioids in the United States, Australia, and Europe throughout the same period.\(^1\) By 2002, more than 5,500 deaths were listed from opioid analgesics, more than either heroin or cocaine.\(^2\) This increase in deaths was mirrored by a similar increase in prescription opioid analgesics dispensed during the same period.\(^3\) Reports from the Drug Abuse Warning Network indicate that abuse-related emergency room visits involving prescription opioids increased by 153 percent from 1995 to 2002, with a further increase of 24 percent through 2005.

In 2007, the Food and Drug Administration Amendments Act (FDAAA) gave the FDA new regulatory powers to impose newer, far-reaching Risk Evaluation and Mitigation Strategies (REMS). For medications with known abuse potential, the FDAAA requires that elements be included in the REMS to optimize safe prescribing and use of the medication. Options include special training or certification for prescribing or dispensing, dispensing under special circumstances, special monitoring, and the use of patient registries.\(^4,5\)

In 2009, the fentanyl buccal soluble film product Onsolis\(^\text{TM}\) was approved. This product was one of the first potent opioid products approved with a REMS prepared under the new FDA requirements. These REMS have several aspects not seen previously with potent opioid products. These include a requirement that prescribers receive special training on the proper use of the product before being authorized to prescribe the product, to provide mandated education to their patients as part of the prescribing process, and to register their patients in a registry and re-register them every 6 months.\(^6\)

The FDA has expressed their interest in expanding more restrictive REMS to long-acting opioids as a group. Primary care physicians prescribe the vast majority of the opioids administered within the context of ongoing patient care. These same physicians have significant time demands placed on them during the course of their professional career. Our study was designed to obtain the views of a group of primary care physicians practicing in Pennsylvania regarding the impact of specific strategies that could be included in a REMS on their willingness to use opioid-containing products to treat pain.

METHODS

The goal of this study was to obtain preliminary information regarding the impact of specific REMS strategies on their willingness to prescribe an opioid product. This study was approved by the University of Pennsylvania Institutional Review Board, which exempted the survey from the requirement to obtain written informed consent from the physicians who participated in the study.

All members of the Pennsylvania Academy of Family Physicians who had provided the academy with a valid e-mail address (N = 2,800) were invited by e-mail on January 8, 2009 to participate in the study. An electronic link to the survey (Table 1) was included in the e-mail. No compensation was offered to physicians who elected to participate in the survey. There were a total of 259 respondents (9.25 percent), of whom, 87 percent described themselves as primary care physicians and the remainder as specialists. Each questionnaire collected demographic information from the respondent regarding the location of their practice, urban or rural, and their current opioid prescribing (Figure 1). In addition, the survey asked physicians to document what they felt their response would be to specific strategies that could be included in a REMS for an opioid product.

RESULTS

Between August 2009 and April 2010, 259 respondents in Pennsylvania completed the survey. The respondents were almost evenly split in terms of their practice location, 48 percent from a rural location (population < 200,000), and 52 percent from an urban location (population > 200,000), with 87 percent of those completing surveys identifying themselves as primary care practitioners and the remainder as specialists.

The vast majority of respondents in our survey are already prescribing opioids as a part of their routine practice; 96 percent for acute pain of 2 weeks duration or less, 77 percent for cancer-related pain, and 83 percent for chronic nonmalignant pain.

Sixty-four percent of the physicians who prescribe opioids for chronic cancer-related or nonmalignant pain require patients to sign opioid agreements (64 percent). However, only 40 percent of these physicians report using urine drug screens as part of their ongoing opioid therapy and 17.8 percent report using periodic pill counts.
Physicians were asked if they would participate in a 2-hour training session to be able to prescribe a new transmucosal fentanyl product for the treatment of cancer-related breakthrough pain. Of these physicians, 48 percent stated that they would, whereas 44 percent stated that they would not. When asked if they would participate in such training to continue to be able to prescribe other transmucosal fentanyl products already on the market, 53 percent of the physicians who currently use these products reported...
that they would participate in such training, whereas 47 percent stated that they would discontinue their prescribing of these products.

Physicians were asked if they would prescribe a transdermal fentanyl product if they were required to participate in mandatory training, complete mandatory patient education for each patient prescribed the medication, register the patient before prescribing the medication, and to re-register the patient every 6 months throughout therapy. Of the respondents, 50.2 percent reported that they would continue to prescribe the transdermal fentanyl product, whereas 49.8 percent reported that they would no longer prescribe the product with these requirements in place.
Physicians were then asked to rate their response to four possible strategies that could be included in a REMS for an opioid product. Ratings were an 11-point categorical scale, where 0 = “no impact on my willingness to prescribe long-acting opioids” and 10 = “I will discontinue prescribing these opioids as part of my practice.” These results are provided in Table 3. Physicians perceive specific strategies to be more burdensome than others. Only 22.2 percent of physicians report being likely to discontinue opioid therapy (score 8-10) if they are required to document ongoing monitoring of therapy including efficacy, safety, and monitoring for aberrant drug-related behavior, whereas 31.2 percent of physicians report being likely to discontinue opioid therapy if they are required to complete 4-8 hours of mandatory physician education followed by 2 hours of pain-related continuing medical education every 2 years. However, the survey did not evaluate the impact of a combination of these strategies on physician willingness to prescribe an opioid product. Survey respondents were allowed to enter comments as free text after completing the survey (Table 2).

**DISCUSSION**

From our survey results, it is clear that the new more restrictive REMS are likely to be a significant deterrent to physicians prescribing potent opioids. A problem that may arise if only certain opioid formulations are singled out for extra restrictions is that prescribers will avoid the extra work involved by using unrestricted opioids that could feasibly be inferior in terms of both benefit and risk. If new restrictions apply only to ultra rapid-onset fentanyl products (as is the current state of REMS), only a minority of all opioid prescriptions will be affected, and there are many alternatives. However, it is proposed that
the more restrictive REMS should be extended to long-acting opioids as a group. Although we may not know with certainty that long-acting opioids provide better analgesia with less risk of addiction than their short-acting counterparts, expert opinion has taught us exactly this over the past decade or so. It seems premature then to discourage the use of long-acting opioids while the research base supporting their use is equivocal. Several of the provisions described in our survey, when taken in isolation, may lead physicians to limit or to not use opioid products subject to the provision. Although such an action may have an impact on the availability of opioids for nonmedical purposes, it may also adversely impact access to these medications for patients with a legitimate medical need.

In a recent report, a large percentage of a physician’s day is spent doing a variety of patient care tasks that are necessary, but are not compensated for. These include returning telephone calls and e-mails, handling prescription refills, and reviewing imaging reports and laboratory studies. Many, if not all, of the options that have already been included in more restrictive REMS or that are under consideration would increase this burden.

New opioid preparations have been approved or are under development that are intended to decrease the risk of diversion or nonmedical use of the product. Payers will soon be asked to pay a price premium for these products due to the perceived benefit that they offer. However, limited data are available to support claims of decreased abuse or diversion.

There are several additional options that can be considered when addressing the very real problem of prescription drug abuse. These include a refocusing of national drug policy away from enforcement to education, prevention, and treatment. In addition,
many policymakers have advocated for increased efforts at education for healthcare providers on the diagnosis and treatment of pain. Legislation was recently passed that authorizes the creation of such an educational program. However, no funding for these provisions has been passed yet, and as a result, this program remains inactive.

This study has several limitations. The survey was distributed by e-mail only to active members of one primary care society. As a result, practicing physicians who are not members and those who did not provide an e-mail address were not invited to participate. In addition, a relatively small percentage of those individuals who were asked to take the survey responded. It is also unclear how many members read the newsletter or had active e-mail addresses in the database. However, the demographics of those who did respond are similar in nature to the overall demographics of the society with regard to practice location and percentage of members who are primary care certified versus specialists. Our survey may however provide interesting preliminary information regarding possible physician reaction to REMS strategies.

Our survey shows that a significant number of physicians currently prescribing opioids may decide to opt out of participating in more restrictive requirements to prescribe to their current levels. Follow-up questionnaires and studies directed toward investigating where these prescribers would advise their patients to go to receive their opioids would be useful. It would also be worthwhile to investigate whether these prescribers intend to simply stop prescribing extended-release opioids to prescribe immediate-release preparations of oxycodone and hydrocodone or if they simply intend to stop prescribing opioids altogether. Until we know more about these unknowns, we hope that decisions being made by regulatory authorities on the future direction of REMS will be made soberly and judiciously.

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REFERENCES