Attention Prescribers: *FDA seeks your help in curtailing the U.S. opioid epidemic*

Summary

- In light of the expanding opioid epidemic in the U.S., FDA urges prescribers to take advantage of training on opioid prescribing, available as of March 1, 2013. This voluntary training will be provided at little to no cost through accredited continuing education activities supported by independent education grants.
- Taking advantage of training opportunities on opioid therapy, now and in the future, is one of three key roles that FDA sees for prescribers in helping to curtail this pervasive problem. The other two are: knowing the content of the most current drug labels for the opioids they prescribe, and educating patients about the appropriate use of opioids, their potential risks, and proper disposal techniques.
- FDA-approved drug labels are frequently updated based on additional science, new benefit-risk information, or public health implications regarding the medication. Labels of extended release and long-acting opioid drugs were changed in July, 2012.

Introduction

Misuse and abuse of prescription opioids has reached epidemic proportions in the U.S. While much of the problem is attributable to illicit use, appropriate use of medications for pain may also lead to unnecessary adverse events, addiction, and death for some patients. *No group can be more effective in reducing this trend than our nation's front-line health care professionals, especially physicians and other prescribers.*

FDA sees three key roles for prescribers in curtailing the U.S. opioid epidemic, 1) ensuring that they have adequate training in opioid therapy, 2) knowing the content of the most current opioid drug labels (examples of the important information found in the labeling of two opioid drugs, OxyContin and Dolophine, are provided at the end of this document), and 3) educating patients about the appropriate use of opioids, their potential risks, and proper disposal techniques.

Take advantage of important training opportunities

As the opioid epidemic has evolved in recent years, extended-release (ER) and long-acting (LA) (ER/LA) opioids have clearly emerged as products with the highest potential for harm, misuse, and abuse. These products contain large amounts of opioids in a single dosage form, sometimes in sufficient quantity to be lethal, especially in children, and they are a prime target of drug abusers.

In July of 2012, FDA approved a Risk Evaluation and Mitigation Strategy or REMS for these products. A REMS is a risk management plan for a manufacturer to implement that

goes beyond the requirements in the drug prescribing information to manage serious risks associated with a drug.

An important element of this REMS is the availability of voluntary ER/LA opioid training programs, at little to no cost, to all U.S. licensed prescribers. The first of these programs is available as of March 1 and more will become available. Although the programs will be funded by opioid product manufacturers, the content will be objective and independent. The programs will be offered by independent providers of continuing medical education (CME) and based on an FDA blueprint that was developed with input from a wide range of stakeholders. Included will be information on weighing the risks and benefits of opioid therapy, the appropriate choice of therapy for each patient, and managing and monitoring patients and counseling them on the safe use of these drugs. The program also will include learning to recognize potential for, and evidence of, opioid misuse, abuse, and addiction, as well as general and drug-specific information about ER/LA opioid analgesics. FDA encourages all opioid prescribers to take advantage of this valuable training to help ensure they have adequate and up-to-date training in opioid therapy.

More information can be found at https://search.er-la-opioidrems.com/Guest/GuestPageExternal.aspx, which will be updated as additional opportunities become available.

Review and know the most current opioid drug labels

The July 2012, REMS for ER/LA opioids also included significant changes to the FDA-approved drug labels for these products. The revisions focused on making the labeling consistent among ER/LA products, and on increasing the prominence of information available regarding risk and precautions, such as those for abuse and misuse, respiratory depression, and accidental exposure.

The drug label, or package insert, that accompanies all FDA-approved medications is the most complete source of information on the drug. Drug labels provide important safety and efficacy information and clinical data to prescribers on the benefits, risks, and appropriate use for *all* FDA-approved drugs. The FDA-approved drug label is one of the most useful tools prescribers have for providing safe and effective opioid therapy to their patients.

As with all FDA-approved drugs, each ER/LA opioid product label has information unique to its own chemical compound and formulation. However, ER/LA opioid labels also share many important similarities. Therefore, maintaining a thorough knowledge of the drug labels can help prescribers inform their decision-making to ensure safe, appropriate, and effective use. Examples of important information available in the FDA-approved labeling for two ER/LA opioids with particular impact on the epidemic -- OxyContin (oxycodone hydrochloride controlled-release) and Dolophine (methadone hydrochloride) -- are provided at the end of this document.

Labeling for all FDA-approved opioids can be found on the Drugs@FDA website, as well as at pharmacies and on many manufacturers' websites. Labeling is also the root source of information prescribers receive from a wide variety of commercial online reference products and other resources educating prescribers about the safe and effective use of FDA-approved drugs.

Keep up with changes to drug labels

It is important to know that drug labels may change as new information on any FDA-approved products becomes available and that these changes occur frequently. We encourage prescribers to regularly review these changes. FDA's MedWatch site provides easy access to safety labeling changes for FDA-approved drugs. This resource clearly identifies the parts of the label that have changed.

Help educate patients to use opioids safely and effectively

Patient education is vital to safe and effective opioid use. FDA urges all prescribers to ensure patients using opioids are appropriately informed of the risks and benefits of these drugs and fully understand directions for their use. The opioid drug labels also provide prescriber information related to patient education.

FDA-approved Medication Guides are key patient education tools. Pharmacies are required to provide them to every patient who receives an ER/LA opioid. Prescribers can also download all available Medication Guides for use in their offices. Among other valuable information, Medication Guides for ER/LA opioids inform the patient on safe disposal of their unused medication. FDA has also created a patient counseling document that prescribers can use to help educate patients on the safe and effective use of opioids.

Conclusion

FDA remains committed to making sure that patients in need have continued access to appropriate pain medications, while also ensuring that all opioid products are used as safely and effectively as possible under the supervision of prescribers armed with sound information and training. Prescribers are critical to successfully curtailing this national problem.

See key examples of useful labeling information on next page.

Two examples of information from ER/LA opioid labels

OxyContin

OxyContin (oxycodone hydrochloride controlled-release) is a product that has received a great deal of public attention in the ongoing problem of opioid misuse, abuse, addiction, and overdose. Much of the risk information in the label for OxyContin also describes risks common to other ER/LA opioids. OxyContin labeling, as with the labels for other ER/LA opioids, begins with a prominently displayed *Boxed Warning*, FDA's highest level of warning for a drug's risk potential. The boxed information highlights three specific warnings:

- The first emphasizes the drug's risk for abuse and addiction and instructs prescribers to monitor patients for signs of these risks throughout their use of the drug.
- The second identifies the risk of fatal respiratory depression and informs prescribers of the need to educate patients on proper administration.
- The third highlights the risk of fatal overdose from accidental ingestion, especially in children.

Despite these prominent warnings, misuse, abuse, addiction, and overdose from intentional and accidental opioid ingestion continue to increase. FDA urges all prescribers to be constantly aware of these *Boxed Warning* risks and especially vigilant in their prescribing practices to help to reduce these serious problems.

Following the *Boxed Warning*, the *Indications and Use* section of the OxyContin label informs prescribers that the drug is FDA-approved for the management of "moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time." Importantly, this section also notes the limitations for use, in particular the specific types of pain treatment for which the drug is not approved. These limitations include: as needed use for intermittent pain, use in acute pain and/or mild pain, and use in most post-operative pain settings. While OxyContin is not specifically contraindicated in these situations, the available data suggest the potential benefit of using OxyContin in these situations may not outweigh its risks. As a result, FDA wants prescribers to be thoroughly informed of the approved uses and limitations of use prior to prescribing any ER/LA opioid.

The Dosing and Administration section for OxyContin provides a range of useful information for initiating, selecting, and maintaining an appropriate dose. In addition, the label notes that higher doses of OxyContin are only appropriate for use in opioid-tolerant patients. For some other ER/LA opioids, all strengths are approved for use only in patients who are opioid tolerant, even the lowest available strength. Another important point in this section, and in the *Dosing and Administration* sections of all of the ER/LA opioid labels, is a reminder to prescribers to continually reassess their patients' needs for ongoing treatment with an opioid based on their levels of pain, their responses to OxyContin, and any problems that develop due to the medication's use.

Like labels for other ER/LA opioids, the OxyContin label, in addition to the *Boxed Warning*, has an entire section devoted to the drug's high potential for abuse and dependence. This section begins with the warning, "Abuse of OxyContin poses a hazard of overdose and death."

A significant number of adverse events and deaths caused by opioids are a result of accidental exposure. This is especially unfortunate when it happens to children. The OxyContin label informs prescribers to instruct patients to securely store the medication and to dispose of unused OxyContin by flushing the tablets down the toilet. This warning and method of disposal applies to all ER/LA opioids. Secure storage also helps to prevent unauthorized access to opioids by family, friends, and other household contacts of patients with valid opioid prescriptions, as many adverse events and deaths continue to occur in people who use opioids prescribed for others.

As mentioned earlier, a key role of the prescriber in helping to curb the nation's opioid problem is to ensure patient education. The OxyContin label dedicates a section to patient counseling information, as do the other ER/LA opioid labels. FDA encourages prescribers to counsel all patients according to this labeling.

Dolophine

Dolophine (methadone hydrochloride) is a long-acting opioid approved for both pain treatment and addiction. It is responsible for a highly disproportionate number of deaths from overdose compared to all other opioids. Like other ER/LA opioids, Dolophine is indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. However, it is also indicated for the detoxification and maintenance treatment of opioid addiction in conjunction with appropriate social and medical services.

Although death from overdose is a significant risk with all ER/LA opioids, methadone accounts for nearly one in three prescription pain medication overdose deaths in the U.S., even though it accounts for only about two percent of the total number of opioid prescriptions filled. Several key characteristics of methadone, discussed below, have led to product labeling for Dolophine that underscores the need for prescribers to have a clear understanding of how methadone differs from other opioids. These key differences include a peak respiratory depressant effect that occurs later and persists longer than its peak analgesic effects, a significantly variable potency relative to other opioids, and known effects on the cardiac QT interval. In addition, many of the deaths associated with the use of methadone for pain management occur due to errors in estimating an appropriate starting dose when physicians convert patients from other opioids to methadone. The Dolophine label was updated to provide greater clarity concerning these and other important safety messages.

OxyContin and Dolophine serve as two useful examples of the particular importance of prescriber knowledge of all ER/LA opioid product labels.