A Difficult Balance — Pain Management, Drug Safety, and the FDA

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Pain is a common medical problem, and relief of pain is an important therapeutic goal. Although nonpharmacologic approaches to treating pain (e.g., behavioral techniques) show promise for certain conditions, pain is most commonly treated with analgesics. Over the past decade, there have been growing concerns about the harm — abuse and addiction, as well as serious injury and death — caused by the use of prescription and over-the-counter analgesics. These concerns have emerged in parallel with the evolving understanding of the importance of pain management in medical care. We at the Food and Drug Administration (FDA) have been engaging physicians, pharmacy groups, patients, and other stakeholders in an ongoing effort to strike the right balance between two important goals: on the one hand, providing access to pain medications for those who need them, and on the other hand, managing the variety of risks posed by analgesic drugs. Recent FDA advisory committee meetings and actions reflect this effort.

Acetaminophen is one of the most commonly used analgesics. In 2008, approximately 25 billion doses were sold in the United States. Acetaminophen is marketed as a single-ingredient drug but can also be found in a multitude of over-the-counter combination products, such as cough and cold medicines, as well as in prescription opioid–acetaminophen combination products (e.g., Vicodin [Abbott], Percocet [Endo Pharmaceuticals], and Darvocet [AAIPharma]). Although acetaminophen, when used as labeled, is generally safe, the ubiquity of the drug and its relatively narrow therapeutic index create the potential for serious harm from both inadvertent and intentional overdoses (for related emergency department visits, see bar graph). Approximately 30,000 hospitalizations are associated with acetaminophen overdose in the United States annually — approximately half of them resulting from unintentional overdose. Acetaminophen is also a leading cause of acute liver failure in the United States.

In June 2009, the FDA held a 2-day public advisory committee meeting to discuss acetaminophen toxicity. The FDA presented multiple options for improving the management of acetaminophen-related risk. The top three recommendations of the committee were to reduce the maximum single dose of over-the-counter acetaminophen from 1000 mg to
In January 2009, the FDA convened an advisory committee meeting to discuss the safety and continued marketing of propoxyphene products. Propoxyphene, a low-potency opioid indicated for mild-to-moderate pain, has been on the U.S. market since 1957. A number of questions had surfaced regarding the safety and usefulness of propoxyphene in today’s armamentarium. In July 2009, the FDA made public its decision to require the makers of propoxyphene-containing products to make changes in safety labeling, including adding a boxed warning and a medication guide to address the risks of overdose, both accidental and intentional. The agency is initiating additional studies of propoxyphene safety.

Although the risks of serious or fatal gastrointestinal bleeding from nonsteroidal antiinflammatory drugs (NSAIDs) have long been recognized, additional safety concerns have also emerged about these agents. In April 2005, the FDA implemented the recommendation of an advisory committee to require a boxed warning on the labels of NSAIDs (except aspirin) about the risk of excess myocardial ischemia, particularly in patients with preexisting heart disease.

Despite increased awareness of the harm resulting from the use of NSAIDs, acetaminophen, opioids, and other drugs for pain, it is likely that extensive prescribing and use of these drugs will continue. Given this reality, there is a need for more vigorous risk-management efforts by the FDA and other stakeholders in the health care system. The FDA cannot address these risks on its own; prescribers and users of analgesics must also participate in this effort. Any risk-manage-
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The number of primary admissions for treatment of abuse of nonheroin opiates or synthetic substances by persons 12 years of age or older from 1997 through 2007 is shown in the graph. The drugs reported to be involved in these episodes include codeine, hydrocodone, hydromorphone, meperidine, morphine, opium, oxycodone, pentazocine, propoxyphene, tramadol, and other drugs with morphineline effects. Nonprescription methadone is not included. Data are from the Treatment Episode Data Set, 1997 through 2007.

Getting to the Real Issues in Health Care Reform

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No issue has dominated the health care reform debate as much as whether the U.S. government should offer a health insurance plan to compete with private insurers — the so-called public option. Congress has discussed two approaches to the public option, one of which would have the public plan pay providers at rates close to Medicare rates (generally, substantially below those of private insurers). Opposition by insurers, providers, and the business community, as well as fears that such a payment structure would lead to a single-payer system, has pushed this “robust” public option off the table. Instead, both the House bill and, presumably, a final Sen-