Proposed FDA Rules on Painkillers in U.S.
Rile Cancer Community

By Vicki Brower

Undertreatment of cancer pain remains a substantial problem, according to a new survey conducted by the American Cancer Society. Published in May, the survey found that 65% of interviewees had moderate or severe pain.

Now, an initiative from the U.S. Food and Drug Administration could make it even more difficult for cancer patients to get adequate pain relief by limiting access to opioids, according to some oncologists.

The impetus for this initiative was the FDA Amendments Act of 2007, which gave the agency authority to require a Risk Evaluation and Mitigation Strategy (REMS) for drugs and biologics if necessary to ensure that the benefits of an agent outweigh its risks. To carry out this mandate, the agency has proposed new rules requiring companies seeking approval for certain drugs—extended-release opioids containing morphine, fentanyl, oxycodone, hydrocodone, and methadone—to present a REMS. If a drug is already on the market, companies must submit a REMS as a condition of its continued sale. And if a company does not satisfactorily fulfill the new REMS requirements, the FDA can pull the drug from the market.

The proposed rules are the FDA’s response to rising rates of prescription opioid diversion, abuse, and overdose, especially by teens and youth in their 20s, and it has the strong support of parent groups. But among oncologists and others in the cancer community, the measure has produced alarm and severe criticism.

“We agree that there are dangers associated with these drugs, but they need to be available for cancer patients and we need to be able to prescribe them,” said Kathleen Foley, M.D., attending neurologist in the pain and palliative care service at New York’s Memorial Sloan–Kettering Cancer Center. With 1.5 million patients diagnosed with cancer each year, two-thirds of whom eventually have advanced cancer pain, and millions of cancer survivors who have treatment-related chronic pain, the availability of opioids is a more significant issue, Foley said.

Others express similarly strong reactions to the FDA’s initiative. “We are terrified about the impact the new regulations will have on our patients,” said Judi Lund Person, vice president of regulatory and state leadership at the National Hospice and Palliative Care Organization in Alexandria, Va. Sean Morrison, M.D., professor of palliative care at New York’s Mount Sinai School of Medicine, acknowledged that abuse of opioids was a problem. “But it is dwarfed by the cancer pain crisis.”

In the FDA’s proposed rules, the REMS program would require that health care providers receive special training, pharmacies and practitioners receive special certification, drugs be given to patients only in certain health care settings, and safe use be documented through lab tests. Patients using these drugs would also have to enroll in a registry.

Still in the formative stage, the REMS initiative was the subject of several meetings this spring between the FDA and stakeholders. Questions for consideration appeared in the April 20 Federal Register. By the time the period of public comment closed on June 30, the agency had received more than 800 submissions, an indication of how seriously stakeholders are taking REMS, said Sidney Scholl, M.D., Ph.D., clinical professor of internal medicine and psychiatry at the Medical College of Virginia in Richmond.

Chilling Effect
Critics of the initiative argue that there is a dearth of evidence showing that risk management strategies are effective in combating drug diversion. “There is absolutely no suggestion from any research that REMS will address abuse,” said Foley. She urges that other methods of restricting the flow of opioids be employed, such as halting Internet sales and educating parents on the safe storage and disposal of these medications at home (diversion from the prescribed patients to young family members accounts for much of the abuse). “Young people and their families should be educated, and patients and drug companies should not be targeted,” she said.

In particular, the possibility of a patient registry rankles Foley, Morrison, and others. “In practice, registries have a huge chilling effect on pain control,” said Russell Portenoy, M.D., chairman of the department of pain medicine at New York’s Beth Israel Hospital. He cited the time and effort involved, the resulting scrutiny and stigmatization of patients, and the likelihood of errors. “There is no evidence that patient registries reduce drug abuse,” he added.

Instead, REMS should include special scrutiny of certain regions known as areas of opioid abuse and have a Web site for complaints and feedback, Portenoy said.

Another alternative to registries, say the critics, is prescription monitoring systems, which 38 states now use. “These are an effective, nonintrusive program, which could be expanded so patients are not swept up into unintended consequences,” Lichtenfeld said. Portenoy added that in the most efficient states, prescribing information is in an online monitoring database, which can be scanned to determine whether patients are getting other controlled substances from other physicians.

Input Into Final Rule
Some, however, are optimistic that the proposed initiative will not compromise patient
care, noting that the community will be able to influence the final regulations. According to the new law, REMS must not pose an unreasonable barrier to patient access to opioids, said Jack Henningfield, Ph.D., professor of psychiatry and behavioral science at the Johns Hopkins University School of Medicine in Baltimore. “The agency is taking its time and doing a good job listening to all constituencies to get diverse input.”

With much at stake, various groups are working to shape the final rule. Drug companies are working together and with the FDA to come up with a REMS for extended-release opioids that will satisfy the agency. Twenty-five companies that produce generic and brand-name opioids have formed an industry working group to develop a REMS that they will submit to the FDA. (The first new opioid drug to have a REMS accepted was Onsolis, an oral transmucosal fentanyl film for breakthrough pain produced by BioDelivery Sciences International in Raleigh, N.C., and approved for marketing in July.)

Foley, Person, and others have joined the American Pain Foundation and formed a Pain Care Task Force, which has issued several other recommendations for the final REMS requirements. Above all, they should not interfere with prescribers’ ability to develop, provide, and adjust pain care management regimens for patients, according to their recommendations. They have petitioned the FDA to develop the rules in such a way that they can be measured to determine their effectiveness in reducing abuse, misuse, and overdose. The group also wants a pilot program to assess the ultimate REMS plan before it is finalized.

Perhaps most important, the group stresses that short-acting opioids should also be subject to REMS to avoid prescribers’ switching to less-regulated, shorter-acting drugs. It also urges that REMS prescriber and dispenser education be tied to the U.S. Drug Enforcement Administration license registration to encourage responsible prescribing and that patient education programs be developed for individual products.

Even as the oncology community has mobilized to help shape the final REMS rules, two separate, more recent actions may exacerbate the problem of patients’ access to opioids. In April, the FDA ordered seven companies to stop producing and distributing several older drugs that predate federal regulation, under the Unapproved Drugs Initiative (of 2006). And in July, an FDA advisory committee voted to remove two combination opioids containing acetaminophen from the market.

In light of these actions, oncologists’ and patients’ choice of pain management drugs may depend even more on what the FDA decides regarding the final REMS regulations. A decision is expected later this year.