

Drugmakers Want Balance Between Safety and Patient Access in Opioid REMS

Although drugmakers are welcoming a final version of a classwide opioid risk evaluation and mitigation strategy (REMS), they believe it should protect patient safety without hindering reasonable access to the products.

"With close monitoring and surveillance, the implementation of the REMS will have the intended effect of reducing abuse without restricting patient access," said King Pharmaceuticals Chief Science Officer Eric Carter.

A draft version of the REMS proposal for extended-release and long-acting opioids released last month avoided mandatory physician and patient training, requirements that some drugmakers thought would hamper physicians' ability to write opioid prescriptions (*DID*, June 30).

Abuse of prescription pain killers is a growing problem in the U.S. A study released Thursday by the Substance Abuse and Mental Health Services Administration showed a 400 percent increase between 1998 and 2008 in the number of substance abuse treatment admissions associated with the abuse of narcotic pain relievers.

In interviews with *DID*, medical officers from two major opioid drugmakers, King Pharmaceuticals and Covidien Pharmaceuticals (formerly Mallinckrodt), said they ultimately view the REMS as a base document from which to work, with drugmakers customizing a REMS for each individual product.

"We don't want the REMS [to be seen] as a one-size-fits-all for every product," noted Covidien Chief Medical Officer Herbert Neuman. "It has to be tailored to each individual product."

In developing the REMS for once-daily Exalgo (hydromorphone HCl extended-release), which launched in April, Neuman said the company went through a failure mode analysis that sought to determine where a patient might be susceptible to abuse "and mitigate those things that could go wrong." That analysis led to the development of a 24-hour timer placed on top of a pill bottle and included in a new patient kit.

"These are the types of things we're doing that would not show up in a classwide REMS," he added.

Carter said that King was the first company to engage in human-abuse liability studies in an effort to curb abuse. All of King's opioid products in development are in

an abuse-deterrent formulation, a trend likely to continue as a result of the classwide REMS and which could prove to be a marketing advantage, he added.

King's Embeda (morphine sulfate/naltrexone HCl) won approval last August and is widely viewed as the first abuse-resistant prescription opioid. If someone chews or crushes the tablet in an effort to get high, naltrexone, a drug commonly used to treat alcoholism, is released, counteracting the effects of morphine.

The company also is seeking approval of Remoxy, an abuse-resistant, controlled-release formulation of oxycodone, which has been held up since the FDA issued a complete response letter in December 2008. However, the company plans a Remoxy resubmission by the end of the year.

The agency notified manufacturers of long-acting and extended-release opioids in February 2009 that their products would require a REMS. Products covered under the proposed classwide REMS include brand-name and generic drugs containing fentanyl, hydromorphone, methadone, morphine, oxycodone and oxymorphone.

The 374-page opioid REMS proposal will be debated at a joint meeting of the FDA's Drug Safety and Risk Management and Anesthetic and Life Support Drugs advisory committees on July 22 and 23.

The REMS proposal and other meeting briefing documents are available at www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndLifeSupportDrugsAdvisoryCommittee/UCM217510.pdf.

— Jonathan Block

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