News From the Food and Drug Administration

New Salvo Against Opioid Abuse

Building on its recent efforts to reverse the US epidemic of opioid abuse, the FDA has issued draft guidance for the pharmaceutical industry to develop generic abuse-deterrent formulations of approved opioid medications.

Last year, the FDA provided the industry with final guidance on developing abuse-deterrent versions of brand-name opioids. "We recognize that abuse-deterrent technology is still evolving and is only 1 piece of a much broader strategy to combat the problem of opioid abuse," FDA Commissioner Robert Califf, MD, said in a statement (http://1.usa.gov/25nAOQN).

The recent draft guidance is aimed at ensuring that a generic version is no less abuse-deterrent than its brand-name formulation. During generic version evaluations, the FDA advised drug makers to consider all potential routes of abuse: parenteral, oral, nasal, and inhalation.

Comparisons of brand-name opioids and their generic forms should use tiered testing that begins with simple ways a solid drug could be altered with common household utensils such as cutting with a knife or shredding with a cheese grater.

Next, in vitro studies should examine whether solvents including water, food-grade vinegar, 40% ethanol, cooking oil, or isopropyl alcohol can release the drug's opioid content for oral ingestion. If in vitro testing isn't reliable, the FDA recommends pharmacokinetic studies (http://1.usa.gov/1LJvO2w).

The agency cautioned, however, that having abuse-deterrent properties doesn't mean abuse is impossible or that those properties necessarily prevent addiction, overdose, or death. Given the cost considerations, encouraging access to generic abuse-deterrent opioids "is an important step toward balancing the need to reduce opioid abuse with helping to ensure access to appropriate treatment for patients in pain," the FDA noted.

Boxed Warning for Most Opioids

In a related step to tackle opioid abuse, the FDA recently announced labeling changes, including a boxed warning, for immediate-release (IR) opioid pain medications. The changes will affect more than 200 opioid-containing products, FDA officials said during a media briefing.

"I can't stress enough how critical it is for prescribers to have the most current information about the potential risks these products pose to both patients and nonpatients," FDA Commissioner Robert Califf, MD, said during the briefing (http://1.usa.gov/1MF96rY).

Boxed warnings will caution clinicians about serious risks of misuse, abuse, addiction, overdose, and death related to IR opioids, which comprise about 90% of opioids on the market. Boxed warnings also caution that prolonged IR opioid use during pregnancy can result in newborns having potentially life-threatening neonatal opioid withdrawal syndrome.

The FDA's revised indication clarifies that IR opioids should be reserved for pain that's severe enough to require opioid treatment in patients who don't respond to or can't tolerate alternatives such as nonopioid analgesics. Updated dosing information also explains more clearly how to determine initial dosages and change dosages during therapy (http://1.usa.gov/1MzXIhg).

In addition, the FDA will require all opioid formulations to include safety information about potentially harmful drug interactions. Updated labels also will explain the potential for developing opioid-induced adrenal insufficiency and androgen deficiency.

Treating and Preventing Anthrax

A new agent used to treat and prevent inhalational anthrax has received FDA approval.

Obiltoxaximab, marketed as Anthim, is given by injection and used with appropriate antibacterial drugs to treat inhalational anthrax, which often is deadly. The condition results from inhaling spores of the *Bacillus anthracis* bacterium.

In the body, the bacteria replicate and produce toxins that cause massive, irreversible tissue injury and death. A monoclonal antibody, obiltoxaximab neutralizes those toxins (http://1.usa.gov/1UJdLzD). Inhalational anthrax is rare but may occur after exposure to infected animals or contaminated animal products.

Anthrax bacteria also are considered a potential bioterrorism threat because the spores resist destruction and can spread if released in the air. "As preparedness is a cornerstone of any bioterrorism response, we are pleased to see continued efforts to develop treatments for anthrax," Edward Cox, MD, MPH, of the FDA's Center for Drug Evaluation and Research, said in a statement.

Obiltoxaximab was approved under the FDA's Animal Rule, which allows drug approvals based on efficacy findings from adequate, well-controlled animal studies when efficacy trials in humans aren't feasible.

In studies examining the drug's effectiveness as treatment and prophylaxis, more animals treated with obiltoxaximab survived exposure to *B anthracis* spores than those given a placebo. More animals treated with obiltoxaximab and antibacterial drugs survived than those who received antibacterial therapy alone.

A safety study in 320 humans showed that the most common adverse events included headache, pruritus, upper respiratory tract infections, and cough. **– Rebecca Voelker, MSJ**