NEWS FROM THE FDA

Liver Injury With Dronedarone

The Food and Drug Administration issued a safety announcement about reports of rare but severe liver injury in patients taking dronedarone, including two patients who had acute liver failure that required transplantation.

Dronedarone (Multaq) is used to treat abnormal heart rhythm in patients who have those symptoms for the past 6 months, according to FDA.

The announcement warned physicians and patients to be alert for signs and symptoms of liver injury or toxicity, including anorexia, nausea, vomiting, fever, malaise, fatigue, right upper quadrant pain, jaundice, dark urine, or itching. Physicians are encouraged to consider ordering periodic hepatic serum enzymes, particularly during the initial 6 months of treatment with dronedarone.

The label's adverse reactions and warnings and precautions sections are being updated to include information about the potential risk of liver injury.

Lower Acetaminophen Doses Sought

The FDA has asked manufacturers of prescription pain products containing acetaminophen to include no more than 325 mg of the drug in each capsule, tablet, or other dosage unit.

According to a safety announcement by the agency, the action was taken to address the ongoing problem of acetaminophen overdose, a leading cause of severe liver injury in the United States.

The FDA requests that manufacturers of these combination products – including Vicodin and Percocet – add a boxed warning to product labels about the potential risk of severe liver injury if acetaminophen is taken in excessive doses or with alcohol.

Manufacturers have until January 2014 to comply with the recommendations, so a shortage of these medications is not anticipated, according to the agency.

The FDA is also asking clinicians to educate their patients about the dangers of acetaminophen overdose and to advise patients to take no more than the maximum daily dose of acetaminophen (4,000 mg).

"For physicians and other health care providers, we want to emphasize that it's important to talk to patients and make sure that they are aware of the risks of using prescription pain medicines with acetaminophen," Dr. Sandra Kweder said during a press briefing.

Currently, prescription acetaminophen products contain up to 750 mg of acetaminophen per dosage unit, but there are no data indicating that more than 325 mg of acetaminophen per unit provides greater pain relief, according to the FDA.

The agency's request does not apply to over-the-counter products, which can contain as much as 500 mg per tablet or capsule in the products marketed as extra strength.

Almost half of acetaminophen-related cases of liver failure in the United States are caused by overdoses from prescription opioid-acetaminophen products, which are among the most commonly prescribed products in the United States, accounting for almost 200 million prescriptions dispensed per year.

Rules on Tobacco Tightened

Certain tobacco products – including cigarettes, roll-your-own, and smokeless varieties – that were introduced or changed in the United States after Feb. 15, 2007, must be reviewed by the FDA to show that they are "substantially equivalent" to existing products, Dr. Lawrence Deyton, director of the agency's Center for Tobacco Products, said in a press briefing.

The FDA action is driven by the Family Smoking Prevention and Tobacco Control Act, which became law in June 2009. The law allows the FDA to regulate tobacco products with the goal of protecting public health.

The substantial equivalence provisions are "meant to ensure that new tobacco products or changes to existing products are evaluated by the FDA before they enter the marketplace and are consumed by millions of people," Dr. Deyton said. "Up to now, tobacco products have been the only mass-consumed products for which users do not know what they are consuming," he said.

The Tobacco Control Act allows tobacco companies to market products that were available after Feb. 15, 2007, if the companies submit at least a preliminary report to the FDA by March 22, 2011, to show that these products are not significantly different from preexisting products. Products in existence before Feb. 15, 2007, are not subject to the new FDA review, said Ann Simoneau, director of the Center for Tobacco Products' Office of Compliance and Enforcement.

New products introduced after March 22 will follow a different regulatory pathway, Dr. Deyton said.

Physicians should know that the FDA is now examining certain tobacco products and that manufacturers are required to submit information to the FDA about the products and changes to them, "particularly if those changes might raise new questions about public health," Dr. Deyton said.

–From staff reports