# Feds Propose Strong Warnings for OTC Drugs

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The Food and Drug Administration is proposing that all over-the-counter analgesic, antipyretic, and antirheumatic drugs carry new, stronger warnings on the potential for hepatic toxicity and gastrointestinal bleeding.

The warnings will be carried on products used by both adults and children, said Dr. Charles Ganley, director of the FDA's Office of Nonprescription Products, in a briefing with reporters.

Currently, manufacturers can choose what language to use and where to place the warnings. The FDA proposal would require standardized language and also dictate where the warnings appear on packaging and in what type size. Dr. Ganley said that the words "liver warning" and "stomach warning" would be in bold type and be listed as the first warning.

All acetaminophen packages will warn that severe liver damage can occur if more than the maximum recommended dosage is taken in 24 hours, if it is taken with other drugs containing acetaminophen, and if the user has more than three alcoholic drinks in a day while using the product, said Dr. Ganley.

There had been an alcohol warning before; now it will be incorporated into the liver warning section, he said.

The word "acetaminophen" will have to be highlighted on the medicine's container and its carton, he said, adding that many consumers aren't aware that a product contains acetaminophen. There will be a similar requirement for the term "NSAID" on aspirin, ibuprofen, naproxen, and ketoprofen containers.

Nonsteroidal anti-inflammatory drugs (NSAIDs) also will carry a bold, large type "stomach warning," cautioning that the risk of GI bleeding is increased for patients over age 60; who have stomach ulcers or bleeding; who are taking a blood thinner, or steroid medication; or another drug containing an NSAID; who have more than three alcoholic drinks a day; and who take it for longer than directed.

While it has been known for decades that acetaminophen is linked to liver damage, and that NSAIDs can cause GI bleeding, the agency has not been able to move quickly in requiring manufacturers to more prominently display warnings, said Dr. Ganley.

OTC drugs have to be addressed as a class through a formal rule-making process, he said. The agency held advisory committee hearings on OTC painkiller safety issues in 2002. This rule is a result of those recommendations, Dr. Ganley said.

Some critics were not satisfied. "What took the agency so long?" asked Dr. Peter Lurie, deputy director of Public Citizen's Health Research Group, in a statement.

Dr. Lurie said that his organization presented data in 2002 showing that there were 26,000 hospitalizations and 450 deaths a year that were attributable to acetaminophen overdoses. The group has pushed for regulations similar to those in the United Kingdom, which limit the number of pills per package and mg per pill.

As part of this proposed rule, the FDA is seeking comment on whether such limitations should be adopted in the United States, said Dr. Ganley. He added that recent research shows there may be an increase in acute liver failure due to acetaminophen. In the paper he cited, researchers found that the annual percentage of acetaminophen-related acute liver failure increased from 28% in 1998 to 51% in 2003 (Hepatology 2005;42:1364-72).

"It is still a great concern to us that this is occurring, and there is a suggestion that it may be increasing," said Dr. Ganley.

There has been no such increase in toxicity seen with NSAIDs. But, said Dr. Ganley, "These drugs are used by tens of millions of people every week in the U.S." Though he said that in general, "they are quite safe," he added that with so many people taking the medications, rare events will be seen more often.

After taking comment through June 2007, the FDA hopes to write a final rule by the year's end, said Dr. Ganley. He would not predict when manufacturers might have to start complying.

The Consumer Healthcare Products Association (CHPA) said that its member companies welcomed the changes. "The reality is, however, that over-the-counter medicines are real medicines with real risks if misused," said CHPA president Linda Suydam in a statement. ■