FDA Targets Unapproved Hydrocodone Products

BY JEFF EVANS
Senior Writer

The Food and Drug Administration has requested manufacturers and distributors of unapproved cough suppressants containing hydrocodone to stop marketing their products or face legal action.

"The industry has been and is well aware that its drugs were and are being marketed illegally, and the industry continues to circumvent the law and put consumers' health at risk. Nonetheless, the CPG [the FDA's Compliance Policy Guide for marketed unapproved drugs] provided the industry with specific notice that any illegally marketed unapproved drug is subject to FDA enforcement at any time," Deborah M. Autor, J.D., said during a teleconference.

This is the sixth time that the agency has requested marketers of unapproved drugs to stop manufacturing and distributing unapproved products since the FDA began a targeted initiative against them in 2006.

The FDA has identified about 200 unapproved prescription antitussive drugs on the market that contain hydrocodone. Only seven prescription hydrocodone-containing cough suppressants are FDA approved: Hycodan (ENDO Pharms), Mycodone (Morton Grove), Tussicaps (Tyco Healthcare), Tussigon (King Pharmaceuticals), Tussionex Pennkinetic (UCB Inc.), Hydrocodone compound (Actavis Mid Atlantic), and Homatropine methylbromide and hydrocodone bitartrate (Actavis Totowa). Other approved cough suppressants do not contain hydrocodone. The agency did not identify any unapproved pain-relief medications containing hydrocodone.

Of particular concern to the agency are unapproved hydrocodone-containing cough suppressants that carry labels with dosing instructions for children as young as age 2 years, because no antitussive containing hydrocodone has been established as safe and effective for children younger than age 6 years. Other unapproved hydrocodone products have omitted important safety warnings and other information on their labeling, according to the FDA.

Hydrocodone-containing products have potential for adverse events such as psychotic behavior and drug abuse; nausea, vomiting, and constipation; cardiac arrest and respiratory depression; hypersensitivity, including pruritus, dermatitis, and pharyngeal edema; and intentional and unintentional overdose, according to the FDA.

More than 400 spontaneous reports of serious adverse events associated with antitussives containing hydrocodone have been reported to the FDA's voluntary MedWatch program since 2005, including deaths due to overdose, although the agency cannot separate out those pertaining to unapproved versus approved products, Dr. Jason Woo, associate director of medical and scientific affairs at the FDA's Office of Compliance, said during the teleconference.

The agency also has had reports of medication errors associated with formulation changes of unapproved hydrocodone-containing antitussives, such as changing the strength of the active ingredient, and reports of confusion over the similarity between the trade names of these unapproved products and other drug products.

"The mix-ups are a particular concern with these products. These products might be confused with one another, leading to dosing problems," said Ms. Autor, director of the Office of Compliance at the FDA's Center for Drug Evaluation and Research. "For example, in our NDC [National Drug Code] Directory ... there are drugs named Histex and drugs named Histinex, and there are also drugs names Histuss HC, Histussin D, and Histussin HC."

Before the FDA approves a trade name for a drug, agency researchers "make sure that we have done everything to prevent … names that sound alike or look alike or might be written alike. When a drug evades the FDA approval process, that entire process is not brought to bear," she added. These similarly named products can contain different ingredients, so that a physician could write a prescription for a product containing one set of ingredients but actually get a similarly named product with different ingredients, Ms. Autor said.

Companies marketing unapproved hydrocodone-containing products that are labeled for use in children younger than age 6 years were required to end manufacturing and distribution of the products by Oct. 31. Marketers of other unapproved hydrocodone-containing products must stop manufacturing them by Dec. 31 and cease further shipment by March 31, 2008. ■