



FDA Takes Action to Ensure Safe Use of Propoxyphene Containing Products

On July 7, 2009 the Food and Drug Administration (FDA) announced that it would allow the continued marketing and sale of propoxyphene containing products on the U.S. market but was taking several actions to reduce the risk of overdose and other adverse effects. Propoxyphene has been available on the U.S. market since 1957 and is most commonly known as either DARVON or DARVOCET-N-100 although generic equivalents have been available for many years. Many experts have long questioned its efficacy in treating mild to moderate pain, believing that its pain-relieving properties are no better than acetaminophen. Now its safe use, especially in the elderly, has been called into question.

According to the FDA, about 21 million prescriptions containing propoxyphene were written in 2007. At the same time there were 503 propoxyphene related deaths, 20% percent of which were classified as suicide. The National Health Service in Great Britain removed the drug in 2005, citing a trail of suicides and accidental overdoses and European Union (EU) drug regulators have just recommended that EU countries follow suit. In addition, the consumer watchdog group PUBLIC CITIZEN petitioned the FDA in February 2006 to remove all propoxyphene containing products from the U.S. market. Lastly, earlier this year (January 30, 2009), on a vote of 14-12, the FDA's own advisory committee recommended a phased market withdrawal of all propoxyphene products. The FDA does not have to follow the recommendations of its advisory committee but generally does.

FDA's proposed actions include the following:

1. The agency is requiring manufacturers to strengthen the labeling of their products, including a boxed warning, emphasizing the potential for overdose when using these products. Manufacturers will also be required to provide a medication guide to patients stressing the importance of using these drugs as directed. All of these proposed changes are to be submitted to the FDA within 30 days.
2. The FDA also ordered the manufacturer, XANODYNE Pharmaceuticals, to perform a new safety study to monitor the cardiovascular effects of higher than recommended doses. This could lead to future regulatory actions.
3. The FDA is working with the Centers for Medicare and Medicaid Services (CMS) to study the safety and prescribing patterns of propoxyphene among the elderly. Specifically, the FDA will be examining the rates of fatalities and hip fractures among elderly patients and compare these rates to those in elderly patients taking other analgesics.
4. The FDA will also be working with the Veterans Administration and possibly one or more of its epidemiology contractors (e.g. Kaiser-California, etc.) to study additional safety aspects of this medication therapy.

In regards to the FDA's decision to continue marketing propoxyphene containing products, Janet Woodcock, MD (Director of FDA's Center for Drug Evaluation and Research, CDER) stated that "at this time, propoxyphene is an acceptable choice for the treatment of mild to moderate pain when taken as directed. When it comes to acetaminophen or opioids, the FDA is constantly balancing benefit vs. risk." The FDA further defended its position by pointing out that there are not a lot of alternative drugs without similar adverse effects.

Lastly, propoxyphene is included on a number of Potentially Inappropriate Drug Use in the Elderly lists (e.g. BEER's, HEDIS, etc.). The general consensus is that while its use in all elderly patients may not be wrong, its relatively poor efficacy and increased risk of adverse effects should prompt providers to seek safer and more effective alternatives. As a consequence of these longstanding safety and efficacy concerns, **BCBSIL** plans on removing propoxyphene containing products from its 2010 Medicare Part D formulary.

Medical providers are asked to monitor their patients carefully for unusual signs and symptoms while taking propoxyphene containing products and to report all suspected adverse drug reactions to the **FDA's MedWatch Program** by phone at 800.FDA.1088, by fax at 800.FDA.0178, by mail at MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, M.D. 20852-9787, or on the MedWatch Web site at www.fda.gov/medwatch.

References:

1. U.S. Food and Drug Administration. FDA Takes Actions on DARVON, Other Pain Medications containing propoxyphene. 7/7/2009, Accessed on 7/7/2009 at: [http:// www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm170769.htm](http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm170769.htm)
2. U.S. Food and Drug Administration. Propoxyphene Questions and Answers. 7/7/2009, Accessed on 7/7/2009 at: <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm170268.htm>
3. Anon. FDA Orders overdose warnings for DARVO CET. Associated Press/AP Online 7/7/2009. Accessed on 7/9/2009 at <http://www.ncpa.yellowbrix.com>
4. Rebelo, K. FDA Adds Stronger Warnings to Propoxyphene. Medscape Medical News, 7/7/2009, Accessed on 7/8/09 at <http://www.medscape.com>