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<http://tinyurl.com/n5rcfr>

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ROCKVILLE, Md -- July 7, 2009 -- The US Food and Drug Administration (FDA) is taking several actions to reduce the risk of overdose in patients using pain medications that contain propoxyphene (such as Darvon or Darvocet). The actions were taken because of data linking propoxyphene and fatal overdoses.

The agency is requiring manufacturers of propoxyphene-containing products to strengthen the label, including the Boxed Warning, emphasizing the potential for overdose when using these products.

These manufacturers will also be required to provide a Medication Guide to patients stressing the importance of using the drugs as directed.

In addition, the FDA is requiring a new safety study assessing unanswered questions about the effects of propoxyphene on the heart at higher than recommended doses.

Findings from this study, as well as other data, could lead to additional regulatory action.

"Physicians need to be aware of the risk of overdose when prescribing these drugs. They should carefully review patient histories and make appropriate treatment decisions based on the warnings and directions stated within the drug's label," said Janet Woodcock, MD, FDA's Center for Drug Evaluation and Research, Rockville, Maryland. "Prescribers and patients should be aware of propoxyphene's potential risks when used at doses higher than those recommended. Therefore, the FDA is requiring manufacturers to provide more information to help physicians and patients decide whether propoxyphene is the appropriate pain therapy."

To further evaluate the safety of propoxyphene, the FDA plans to work with several groups including the Centers for Medicare & Medicaid Services and the Veterans Health Administration to study how often the elderly are prescribed propoxyphene instead of other pain relievers and the difference in the safety profiles of propoxyphene compared with other drugs.

Propoxyphene manufacturers are required to submit the requested safety labelling changes to the FDA within 30 days, or to provide a reason why they do not believe such changes are necessary. If they do not submit new language, or if the FDA disagrees with the language the companies propose, the Food, Drug, and Cosmetic Act provides strict timelines for discussions regarding the changes. At the end of these discussions, the FDA may issue an order directing the labelling changes as deemed appropriate to address the new safety information.

Also today, the FDA denied a citizen petition from the public interest group Public Citizen requesting a phased withdrawal of propoxyphene. The agency said in its response that despite the FDA's serious concerns about propoxyphene, the benefits of using the medication for pain relief at recommended doses outweighs the safety risks at this time.

The FDA also noted that it plans to further evaluate the safety of propoxyphene and will take additional regulatory action if necessary.

Details of this decision can be found here.

The most frequent side effects of propoxyphene include light-headedness, dizziness, sedation, nausea, and vomiting.

SOURCE: US Food and Drug Administration

Details of this decision:

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm170268.htm>

Propoxyphene Questions and Answers

What is propoxyphene?

Propoxyphene is an opioid medicine that has been marketed in approved drugs such as Darvon and Darvocet since 1957. Propoxyphene is used to relieve mild to moderate pain.

What action is the FDA taking today?

Based on data submitted and available to the FDA, the Agency is acting on its concerns about an increased risk of fatal overdose when using medicines that contain propoxyphene.

FDA is requiring the manufacturers of propoxyphene-containing products to strengthen the label's boxed warning to address the risk of overdose with these products. These manufacturers will also be required to develop a Medication Guide, which is FDA-approved labeling that must be given to patients with each prescription or refill.

Physicians need to be aware of the risk for overdose when prescribing these drugs. They should carefully review patient histories and make appropriate treatment decisions based on the warnings and directions stated within the drug's label.

FDA plans to seek additional data to further evaluate the safety of propoxyphene-containing products and will take appropriate regulatory action as warranted.

Why is FDA taking this action?

FDA is aware of evidence of fatal overdose, both accidental and intentional, involving propoxyphene. In Europe, there is recent evidence that this medication may be more lethal in overdose than other pain medications. FDA is taking action to reduce the likelihood of such fatal overdoses in the United States while we investigate the safety of propoxyphene more fully.

If the FDA is concerned with the safety of propoxyphene-containing products, why not remove them from the market?

Based on all evidence available to the agency, FDA has concluded that the benefits of propoxyphene for pain relief at recommended doses outweigh the safety risks at this time. Therefore, the FDA is not proposing removal of propoxyphene products from the U.

S. market.

FDA recognizes that there are unanswered questions about the safety of propoxyphene when used at doses higher than recommended in the label. These unanswered questions include the effects on the heart in overdose.

Accordingly, we are requiring the manufacturer to conduct a safety study of the effects of propoxyphene on the heart, at higher than recommended doses. In addition, FDA plans to work with other Federal agencies (e.g., Centers for Medicare and Medicaid Services (CMS), Department of Veterans Affairs (VA)) to conduct additional studies regarding the safety of products that contain propoxyphene as compared to other commonly used pain medications.

The following studies are in the planning stages or under discussion:

FDA is working with CMS to study the safety and prescribing patterns of propoxyphene among the elderly. Specifically, FDA will examine the rates of fatalities and hip fractures among elderly patients taking propoxyphene-acetaminophen and compare these rates to those in elderly persons taking other analgesics.

FDA plans to discuss a study examining the safety of propoxyphene-acetaminophen with the Veterans Administration, using the VA's databases.

FDA is planning to examine the feasibility of studying the safety of propoxyphene with one or more of its epidemiology contractors (Vanderbilt University, Kaiser - California, the HMO Research Network at Harvard Pilgrim Health, and Ingenix).

FDA will examine the possibility of reviewing Medical Examiner data in the Substance Abuse and Mental Health Administration's (SAMSHA) Drug Abuse Warning Network (DAWN).

EMA, Public Citizen, and FDA's own advisory committee by a 14-12 vote, recently recommended a phased market withdrawal of propoxyphene products. Why has FDA reached a different decision?

There are differences in how FDA and those who support the market withdrawal of propoxyphene view the benefit and safety data of this drug. FDA finds there is evidence that propoxyphene can effectively treat pain at recommended doses. FDA also finds that the differences in use patterns between Europe and the United States limit the applicability of the European data to the U.S. population. The U.S. data available to date do not confirm the European findings. Because these data are limited, however, FDA is further investigating the safety concerns with propoxyphene in the United States.

While this investigation is occurring, FDA is taking other actions to promote the safe use of propoxyphene.

Are there other medicines available to treat pain?

Yes. Pain is one of people's most common medical complaints. In addition to propoxyphene containing products, pain can be treated with other narcotic-based drugs (e.g., oxycodone and codeine). Further, pain can be treated with aspirin, acetaminophen, ibuprofen, and other drugs. All pain medicines have side effects. Aspirin can cause bleeding of the stomach and intestines and other serious problems. Acetaminophen, the main ingredient in Tylenol and other drugs, can cause liver damage. Codeine, one of the most widely used opioids, can cause severe constipation. It is important that healthcare professionals and consumers be aware of all the risks associated with pain medications, including propoxyphene, when making decisions on how to treat pain.

Additional Information on Today's Action:

[FDA Response to Citizen Petition](#)

[List of References](#)

[FDAAA Letter and Label](#)

[Darvocet Label](#)