



Food and Drug Administration
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Advisory Committee and the Drug Safety and Risk
Management Advisory Committee

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**ASHP Recommends that FDA Withdraw Propoxyphene
From the United States Market**

Good morning. My name is Cynthia Reilly and I am the Director of the Practice Development Division at the American Society of Health-System Pharmacists (ASHP). ASHP represents pharmacists who practice in hospitals and health systems. The Society's more than 35,000 members include pharmacists and pharmacy technicians who practice in a variety of health-system settings including inpatient, outpatient, home care, and long-term-care. I appreciate the opportunity to present the views of ASHP on appropriate regulatory action relating to propoxyphene-containing products.

ASHP policy advocates that the Food and Drug Administration (FDA) withdraw propoxyphene from the United States market based on the drug's poor effectiveness and safety profiles, and because more effective and safer alternatives are available to treat mild to moderate pain.

Propoxyphene has been used for treatment of mild to moderate pain, but it is inadequate for managing severe pain. A meta-analysis of 26 randomized, controlled studies of 2231 patients with postoperative, arthritis, or musculoskeletal pain that compared the effectiveness of acetaminophen plus propoxyphene with that of acetaminophen alone, or placebo, demonstrated that the addition of propoxyphene napsylate 100 mg to patients' pain regimen was no more effective than using acetaminophen alone. Similarly, an evaluation of patients with moderate to severe post-operative pain found that propoxyphene-acetaminophen combination therapy had only similar effectiveness compared to tramadol 100 mg, but was less effective than ibuprofen 400 mg at controlling pain for four to six hours.

While less than 1% of patients taking the recommended dosage of propoxyphene experience adverse effects, some patient populations, such as the elderly and those with

kidney and liver disease, are at greater risk. Use of propoxyphene in these populations represents the greatest potential for patient harm. Propoxyphene has been listed among drugs and drug classes defined by the Beers Criteria and Zhan Criteria as potentially inappropriate medication for older adults, because the drug offers few advantages over acetaminophen while potentially causing the adverse effects associated with opiate analgesics. Elderly patients taking propoxyphene who experience central nervous system effects may be prone to falls that result in bone fractures, including hip fractures that can lead to significant morbidity and mortality. Studies have demonstrated that propoxyphene is commonly prescribed for elderly patients, especially those living in nursing homes. An assessment of prescribing practices for 21,380 nursing homes residents with persistent pain found that propoxyphene was prescribed for 18% of patients. It should be noted that propoxyphene is not recommended for treatment of chronic, or persistent, pain. Extended use of the drug places this already vulnerable patient population at greater risk of harm.

Based on the Beers criteria, the National Committee on Quality Assurance included propoxyphene in a list of medications to avoid in the elderly in the 2006 Health Plan Employer Data and Information Set. The avoidance of propoxyphene has also been recommended by the Agency for Healthcare Research and Quality, the Veterans Health Administration, and other health systems as a strategy to improve patient safety. These efforts have resulted in moderate increases in healthcare professional awareness about the potential for patient harm. However, inappropriate prescribing of propoxyphene remains widespread and is unlikely to change in the absence of a requirement that the drug's manufacturers participate in enhanced surveillance activities and provide education to healthcare professionals and patients.

In summary, ASHP believes that the usefulness of propoxyphene to treat pain is limited, and that the possible risks clearly outweigh any potential benefit. A number of alternative analgesic therapies have demonstrated superior effectiveness and safety for the treatment of mild to moderate pain. Prescribing patterns for propoxyphene also indicate that the drug is commonly inappropriately prescribed for patients and indications for which it is not recommended that increase the risk of patient harm. Based on this evidence, the Society encourages the complete withdrawal of propoxyphene from the U.S. market.