

Acetaminophen Combination Products

IMPORTANT NOTICE

On January 13, 2011, the U.S. Food and Drug Administration (FDA) released a new drug safety communication asking drug manufacturers to limit acetaminophen (Tylenol®) content when combined with other medications in a single product. The communication requested manufacturers of pain relievers containing acetaminophen restrict the amount of acetaminophen to no more than 325 mg per tablet or capsule due to concerns for drug-related liver damage.

BACKGROUND

This action stems from a June 2009 FDA advisory meeting where recommendations presented to the agency included adding a boxed warning, withdrawing prescription products containing acetaminophen from the market, and reducing the acetaminophen component of prescription analgesics. In an effort to determine the significance of the relationship between the use of high-dose acetaminophen and the presence of liver damage, the FDA has analyzed several clinical studies over the past few years. The agency now believes that roughly half of all acute liver failure in the United States in the recent past may have been due to acetaminophen-related over-utilization.

For background information, [click here](#) to review PMSI's Drug Advisory on Acetaminophen Combination Products issued in July 2009.

NEW DEVELOPMENTS

As a result of this new data, the FDA is granting drug manufacturers three years to limit the amount of acetaminophen in all prescription combination products to 325 mg or less. The FDA believes this will give manufactures sufficient time to reformulate their products and submit them for approval. In addition, the agency is requiring the presence of a boxed warning on all prescription acetaminophen products indicating the risk for drug-induced liver toxicity as well as a new warning regarding the possibility of rare allergic reactions. Over-the-counter (OTC) products are not subject to the FDA's new dosage limitations and will remain unaffected at this time. Future actions may be taken for these products as part of the agency's OTC monograph review process.

ECONOMIC IMPACT

The FDA believes the proposed limitation will not significantly impact the level of pain relief available to patients as indicated by a lack of clinical data demonstrating increased efficacy with acetaminophen doses exceeding 325 mg. Although the agency's action will limit the amount of acetaminophen present in prescription combination products, the total number of dosage units and/or the frequency of administration for these agents will not be affected.

IMPACT IN WORKERS' COMPENSATION

Pain medications containing acetaminophen are the most commonly dispensed drugs in workers' compensation. In 2010, 22% of all medications processed by PMSI were combination products containing opioids and acetaminophen. Approximately half of these prescriptions were for products containing more than 325 mg of acetaminophen per tablet/capsule. With few exceptions, the average wholesale price (AWP) of products with 325 mg or less acetaminophen per tablet is 8 to 40% higher than products with more acetaminophen. This could significantly increase spend for these products in the coming years.

NEXT STEPS

PMSI Next Steps

Since this alert does not represent an immediate withdrawal or recall of a product, it does not necessitate changes to PMSI's formularies, quarantine of medications, or prescriber notifications. PMSI anticipates that over the next three years, prescribers will begin gradually converting their injured workers' therapies to the products with lower acetaminophen contents as prescriptions are refilled. This gradual conversion will help to reduce the risk of shortages of the lower strength formulations.

Patient Next Steps

In an effort to address drug-related concerns the FDA has indicated that **patients** should:

- Continue taking prescription combination products as directed by their prescriber.
The agency considers acetaminophen products to be safe and effective when used as directed.
- Do not use more than the recommended maximum daily dose of acetaminophen (4,000 mg per day).
- Do not use more than a single product containing acetaminophen.
- Do not drink alcohol when taking acetaminophen-containing medications.
- Seek immediate medical help if you think you have taken more than the recommended amount of acetaminophen or if a medication-related allergic reaction is experienced.

Prescriber Next Steps

The FDA indicates that **prescribers** should:

- Educate patients about the importance of not utilizing more than 4,000 mg of acetaminophen per day.
- Educate patients to avoid alcohol while utilizing acetaminophen products.
- Report acetaminophen-related adverse events to the agency's MedWatch program.

CONCLUSION

This PMSI Drug Advisory is made available by our clinical pharmacist team to provide you pertinent drug information and identify the potential impact on your injured workers' care and your costs. As your pharmacy partner, PMSI understands the importance of staying on top of breaking news in the pain management arena and keeping you informed. We will continue to monitor and regularly communicate our proactive response to FDA recommendations to help protect your interests.



Proven Solutions for Cost Containment

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REFERENCES

FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure. U.S. Food and Drug Administration. <http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm#references>. <Accessed January 13, 2011>

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