



American Pain Foundation

## **FDA Panel Recommends Market Removal of Opioid plus Acetaminophen Preparations Causing Concern for Individuals Living With Pain**

### **Q&A on Acetaminophen and Opioids**

**Revised: Sept 14, 2009**

Acetaminophen has been on the market for over 50 years and alone is used to treat mild pain and fever. On June 30, 2009, a Food and Drug Administration (FDA) Advisory Committee released recommendations to limit acetaminophen dosages in over the counter (OTC) preparations due to the growing risks of liver damage. This committee was charged to identify ways to lessen this serious health effect associated with acetaminophen, one of the most widely used medications in the U.S. Adult and pediatric OTC formulations of acetaminophen vary in dosing ranges. It is available in a large variety of familiar preparations for minor pain and headache, like regular strength (Tylenol), “extra-strength” (Tylenol ES), a variety of sinus and allergy brands, and cold and cough remedies as well as prescription pain medications for the treatment of mild to moderate pain. This FDA panel of experts voted 36-1 that any preparation on the market should carry a black box warning, the most serious safety label available. Additionally, the panel voted 20-17 for the removal from the market all combination opioid medications that contain acetaminophen. The most common of these preparations are oxycodone+acetaminophen (Percocet, Tylox) and hydrocodone+acetaminophen (Vicodin, Lortab).

**Q:** *Why is acetaminophen combined with opioids in some formulations?*

**A:** Acetaminophen was added to opioid preparations for several reasons:

1. For convenience, because it is easier to take one combined pill rather than two.
2. As a chemical partner so that together pain relief could match what a higher dose of opioid could achieve alone. For example, 7.5 mg of hydrocodone+acetaminophen (classified as a Schedule III Controlled Substance: less restrictive) would equal the effect of one 15 mg dose of hydrocodone (which would be required to be classed as a Schedule II Controlled Substance: more restrictive).
3. It was originally believed that in combination, the medication would be less desirable to substance abusers. However, research has shown that hydrocodone+acetaminophen has ranked highest in the list of misused or abused prescription pain medications over several years. Oxycodone+acetaminophen is not far behind.

**Q:** *Can acetaminophen combined with opioids be risky to my health?*

**A:** At recommended doses acetaminophen does not cause problems, such as stomach discomfort and bleeding, and acetaminophen is considered safe when used according to the directions on its OTC or prescription labeling. However, taking more than the recommended amount can cause liver damage, which can range from abnormal liver function blood tests, to acute liver failure, and even death. Many cases of overdose are caused by individuals who inadvertently take more than the recommended dose (i.e., 4 grams a day) of a particular product, or by taking more than one product containing acetaminophen (e.g., an OTC product and an prescription medication containing acetaminophen). Panel experts cited FDA data that showed approximately 60 percent of acetaminophen-related deaths were related to prescription products.

Liver injury is related to the production of a toxic end-product when acetaminophen is broken down by the body (metabolized). The toxin binds with liver proteins that cause cell injury or cell death. Those with healthy, young and mature livers can remove the toxins more quickly and limit the amount of liver injury as compared to those not so fortunate. Drinking alcohol can slow the removal of toxins even more.

**Q:** *What are the signs of liver failure?*

**A:** Liver failure is a life-threatening condition and demands immediate medical care. Chronic liver failure occurs gradually over time. Acute liver failure occurs suddenly and progresses rapidly (in as little as 48 hours) yet can be difficult to detect initially. The initial symptoms of liver failure are often those commonly seen with a number of conditions, making this challenging to diagnose. Early symptoms include:

- Nausea
- Loss of appetite
- Fatigue
- Diarrhea

As liver failure progresses, the symptoms become more serious.

- Jaundice (Yellow to orange discoloration of the skin and mucous membranes—mouth, eyes, stools)
- Bleeding easily
- Swollen abdomen
- Mental disorientation or confusion (known as hepatic encephalopathy)
- Sleepiness
- Loss of Consciousness and Coma

**Q:** *Could this FDA recommendation be good news?*

**A:** This action could be problematic. All medications have some risk and it is important that the benefit outweighs the risk. Though change can be difficult, safety should outweigh convenience. Not knowing if you are taking too much acetaminophen can be dangerous. It is important to use this opportunity to discuss your risk with your pain care provider based on the amount of acetaminophen that you are taking by prescription and over the counter.

However, the currently approved maximum daily dose of **4 grams/day (1 gram/dose) is safe and effective** and has *not* been associated with liver injury. Acetaminophen has been recognized as generally safe and effective for decades and is associated with few adverse effects when **taken as directed**.

Limiting acetaminophen in a single dose option or lowering the maximum daily dose recommendation, could lead individuals to either experience more pain or try to compensate by taking more of pills at one time, switch to alternative therapies, or both. This could heighten the potential for unintentional overdose as well as lead to the use of alternative medications, such as over the counter NSAID's, which are known to be associated with higher risk than acetaminophen.

**Q:** *I am currently taking Vicodin [Percocet] for the management of my pain. What should I do now?*

**A:** Your first reaction may be “great, now the government is trying to take away my pain medication” or “this is the only pain medication that my doctor will give me” or “I finally found a medicine that works and now it’s gone.”

First: The FDA has not acted on the recommendation from the advisory committee. Right now, they are still available. APF will monitor for their actions.

Second: Plan ahead. You have time to discuss your options with your healthcare professional, should the FDA decide to remove these combination opioid products from the market. This is the time to look at your risks of acetaminophen exposure. You may be surprised at how much you are taking when you add your prescription opioids, OTC headache, allergy or sinus pills, OTC pain relievers for arthritis or minor aches/strains/sprains, etc. Talk with your pain care provider about lowering your exposure to acetaminophen. Take advantage of this opportunity, it may not be a terrible situation as you first thought.

- If you are taking a hydrocodone+acetaminophen product (Vicodin, Lortab, Lorcet), a trial of Vicoprofen or Hycodan (used as a cough medication) might be considered or a change to another opioid or opioid- like medication {unfortunately, there is no plain hydrocodone on the market};
- If you are taking an oxycodone+acetaminophen product (Percocet, Tylox), a trial of plain oxycodone (OxyIR, generic oxycodone, Roxicodone, OxyFast) might be considered or a change to another opioid or opioid- like medication.
- Talk about other treatment options, see:  
<http://www.painfoundation.org/Publications/TreatmentOptions2006.pdf>.