Upcoming Changes to Acetaminophen-Containing Opioid Products

In January 2011, the FDA announced that drug manufacturers will be required to limit the strength of acetaminophen (APAP) contained in prescription drug products to 325 mg per tablet, capsule, or other dosage unit. The FDA believes that limiting the amount of acetaminophen per dosage unit may reduce the risk of severe liver injury from overdosing, and thus limit subsequent cases of liver failure, liver transplant and death. The FDA is also requiring manufacturers to add a *Boxed Warning* highlighting the potential for severe liver injury and a *Warning* about the potential for severe allergic reactions to the label of all prescription drug products containing acetaminophen.

All manufacturers of acetaminophen-containing prescription products must comply with these ***changes by January 14, 2014***. Several products containing opioids in combination with acetaminophen are affected by the mandate, including hydrocodone/APAP (Vicodin®, Lortab®) and oxycodone/APAP (Percocet®). Abbott Laboratories, manufacturer of Vicodin® products, introduced their branded products with the reduced strength of 300 mg of APAP at the end of 2012. Abbott discontinued production and distribution of prior Vicodin® formulations; only the new formulation is available. Prescriptions written for Vicodin®, Vicodin ES®, and Vicodin HP® can no longer be filled with a generic substitute and will be filled as follows:

- Vicodin® (hydrocodone bitartrate and acetaminophen tablets, USP) 5 mg/300 mg
- Vicodin ES® (hydrocodone bitartrate and acetaminophen tablets, USP) 7.5 mg/300 mg
- Vicodin HP® (hydrocodone bitartrate and acetaminophen tablets, USP) 10 mg/300 mg

Prescribers must order hydrocodone/acetaminophen in a generically available strength (example: 5 mg/325 mg tablets). All orders written for "Vicodin" will be filled with the new brand-only formulation.

See table below for existing products affected by the mandate. Shortages may occur as manufacturers are discontinuing and reformulating certain products. Check with local dispensing pharmacies for available products during these changes. Patients who still possess old formulations may continue to take non-expired doses as prescribed under an active prescription, but will need a new prescription once the old formulation is discontinued.

Additional information for Healthcare Professionals:

The maximum amount of acetaminophen in a prescription tablet, capsule, or other dosage unit will be limited to 325 mg. However, the total number of tablets or capsules that may be prescribed and the time intervals at which they may be prescribed will not change as a result of the lower amount of acetaminophen. For example, for a product that previously contained 500 mg of acetaminophen with an opioid and was prescribed as 1-2 tablets every 4-6 hours, once reformulated to contain 325 mg of acetaminophen, the dosing instructions can remain unchanged.

- Advise patients not to exceed the acetaminophen maximum total daily dose (4 grams/day).
- Severe liver injury, including cases of acute liver failure resulting in liver transplant and death, has been reported with the use of acetaminophen.
- Educate patients about the importance of reading all prescription and OTC labels to ensure they are not taking multiple acetaminophen-containing products.
- Advise patients not to drink alcohol while taking acetaminophen-containing medications.
- Rare cases of anaphylaxis and other hypersensitivity reactions have occurred with the use of acetaminophen.
- Advise patients to seek medical help immediately if they have taken more acetaminophen than directed or experience swelling of the face, mouth, and throat, difficulty breathing, itching, and rash.
- Report adverse events to FDA's MedWatch program, *http://www.fda.gov/Safety/MedWatch*

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Text of FDA required Black Box Warning for all acetaminophen-containing prescription products.
These products contain acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4,000 milligrams per day, and often involve more than one acetaminophen-containing product.

Acetaminophen-Containing Opioid Products Affected by the FDA Mandate
The following products contain more than 325mg of APAP per dosage unit and may be reformulated or discontinued prior to January 14, 2014.

Strength (Opioid/APAP)	Dosage Form	Generic Available	Brand Name
Hydrocodone Bitartrate and Acetaminophen Products			
2.5 mg/ 500 mg	Tablet	Yes	n/a
5 mg/ 400 mg	Tablet	No	Zydone®
5 mg/ 500 mg	Capsule	Yes	Stagesic™
5 mg/ 500 mg	Tablet	Yes, *Vicodin® now brand only*	Co-Gesic®
			Lortab® 5/500
			Vicodin® ***Reformulated 2013***
7.5 mg/ 400 mg	Tablet	No	Zydone®
7.5 mg/ 500 mg per 15mL	Elixir	No	Lortab® Elixir
7.5 mg/ 500 mg per 15mL	Solution	Yes	n/a
7.5 mg/ 500 mg	Tablet	Yes	Lortab® 7.5/500
7.5 mg/ 650 mg	Tablet	Yes	Lorcet® Plus
7.5 mg/ 750 mg	Tablet	No	Vicodin® ES ***Reformulated 2013***
10 mg/ 400 mg	Tablet	No	Zydone®
10 mg/ 500 mg	Tablet	Yes	Lortab® 10/500
10 mg/ 650 mg	Tablet	Yes	Lorcet® 10/650
10 mg/ 660 mg	Tablet	No	Vicodin® HP ***Reformulated 2013***
10 mg/ 750 mg	Tablet	Yes	Maxidone®
Oxycodone Hydrochloride and Acetaminophen Products			
5 mg/ 400 mg	Tablet	No	Magnacet®
5 mg/ 500 mg	Caplet	No	Roxicet™ 5/500
5 mg/ 500 mg	Capsule	Yes	Tylox®
7.5 mg/ 400 mg	Tablet	No	Magnacet®
7.5 mg/ 500 mg	Tablet	Yes	Endocet®
			Percocet®
10 mg/ 400 mg	Tablet	No	Magnacet®
10 mg/ 500 mg	Tablet	No	Xolox®
10 mg/ 650 mg	Tablet	Yes	Endocet®
			Percocet®

References:

1. PL Detail Document, Limits to acetaminophen content in prescription combo products. Pharmacist's Letter/Prescriber's Letter July 2012; 280711
2. U.S. Food & Drug Administration (FDA). 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. Accessed May 20, 2013. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm
3. U.S. Food & Drug Administration (FDA). Questions and answers about oral prescription acetaminophen products to be limited to 325mg per dosage unit. Accessed May 20, 2013. Available at: http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm239871.htm

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