abbvie

Date: 07/01/2013

To: Tanja Battle

RE: Changes to AbbVie's Vicodin® (hydrocodone bitartrate and acetaminophen tablets, USP) formulations, which have become generic products with reduced acetaminophen content

Dear Ms. Battle:

This communication is to inform you of two key changes to AbbVie's Vicodin formulations and potential dispensing errors that may warrant your attention. Before explaining these changes, there are a couple of points to communicate regarding Vicodin products. As you may know, VICODIN® **5 mg/300 mg**, VICODIN ES® **7.5 mg/300 mg**, and VICODIN HP® **10 mg/300 mg** (hydrocodone bitartrate and acetaminophen tablets, USP) tablets are indicated for the relief of moderate to moderately severe pain. It is also important to note a **safety consideration** related to hepatotoxicity: acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most cases of liver injury are associated with doses that exceed 4000 mg/day.[1]

On January 13, 2011, the U.S. Food and Drug Administration (FDA) asked drug manufacturers to limit the strength of acetaminophen in prescription drug products, including combination acetaminophen and opioid products, to no more than 325 mg per tablet, capsule, or other dosage unit. The FDA has stated that limiting the amount of acetaminophen per dosage unit in prescription products may reduce the risk of severe liver injury from acetaminophen overdosing.[2] (Please visit the FDA website for more information on acetaminophen dosing: http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm)

Please see Important Safety Information, including BOXED WARNING on hepatotoxicity, on pages 4-5.
Please see accompanying Full Prescribing Information.

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As a result of this mandate, in May 2012, Abbott (now AbbVie) discontinued the manufacturing and distribution of its original formulations of Vicodin (VICODIN® 5 mg/500 mg, VICODIN ES® 7.5 mg/750 mg, and VICODIN HP® 10 mg/660 mg), which contained higher strengths of acetaminophen. **In October 2012, Abbott (now AbbVie) introduced into the market a reformulated Vicodin that is a generic and contains 300 mg of acetaminophen per tablet together with varying strengths of hydrocodone.**

AbbVie's Vicodin reformulations have each been introduced as generic products. This means that patients will pay a generic co-pay for AbbVie's Vicodin products and the retailer/pharmacy will be reimbursed for a Tier 1 generic, even though the products retain the "Vicodin" trade name that was previously associated with the original branded Vicodin formulations.

Additionally, AbbVie's reformulated Vicodin has different National Drug Code (NDC) numbers that are not interchangeable with the NDCs of the original Vicodin formulations. The NDCs for the original Vicodin formulations have been delisted, as those products were discontinued approximately one year ago.

Prescribers sometimes write prescriptions for the hydrocodone/acetaminophen combination as "Vicodin," "Vicodin ES," or "Vicodin HP" and do not include specifics for product strength.[3] It has come to our attention that some of these prescriptions are being filled with product that contains acetaminophen content other than 300 mg, the strength contained in the reformulated Vicodin. These pharmacists are also reporting that they are making this substitution without consultation with the prescribing physician.[3]

According to the FDA, drug products are considered pharmaceutical equivalents if they are identical with regard to active ingredients, dosage form and route of administration, and strength or concentration.[4]

In both Orange Book states and Professional Judgment states, pharmacists are required to call the prescriber before dispensing any product that is not a pharmaceutical equivalent to the product prescribed.

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When pharmacists receive a prescription for Vicodin, Vicodin ES, or Vicodin HP and the strength is not included, the pharmacist should dispense a product containing 300 mg of acetaminophen or call the prescribing physician to clarify. In addition to AbbVie's Vicodin, there are at least two other distributors with FDA-approved products that contain hydrocodone and 300 mg acetaminophen. Dispensing a hydrocodone/acetaminophen product that contains an acetaminophen strength associated with the original Vicodin will result in patients receiving an additional amount of acetaminophen that may not have been intended by the prescriber. According to the FDA, acetaminophen can cause serious liver damage if more than directed is used.[2]

RX WRITTEN[1]	IF YOU DISPENSE: (INSTEAD OF A SUBSTITUTABLE 300 MG ACETAMINOPHEN TABLET) HYDROCODONE/ ACETAMINOPHEN	EXCESS ACETAMINOPHEN PER TABLET	EXCESS ACETAMINOPHEN PER DAY AS PER MAXIMUM DAILY DOSE
Vicodin or Vicodin 5	5 mg / 500 mg[5]	200 mg	1,600 mg
Vicodin ES or Vicodin 7.5	7.5 mg / 750 mg[6]	450 mg	2,700 mg
Vicodin HP or Vicodin 10	10 mg / 660 mg[7]	360 mg	2,160 mg

AbbVie is committed to patient safety and to providing appropriate access to its products. We continue making efforts to ensure that pharmacists are aware of the changes to the Vicodin product line, and we appreciate any assistance you can provide in educating pharmacists in order to address any potential dispensing errors that may be occurring. AbbVie thanks you for your support—please consider disseminating this information to members of the state board, inspectors, and pharmacists as you deem appropriate.

INDICATION[1,5-7]

VICODIN® **5 mg/300 mg,** VICODIN ES® **7.5 mg/300 mg,** VICODIN HP® **10 mg/300 mg,** VICODIN® **5 mg/500 mg,** VICODIN ES® **7.5 mg/750 mg,** and VICODIN HP® **10 mg/660 mg** (hydrocodone bitartrate and acetaminophen tablets, USP) tablets are indicated for the relief of moderate to moderately severe pain.

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IMPORTANT SAFETY INFORMATION[1,5-7]

BOXED WARNING

HEPATOTOXICITY: 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 4000 MILLIGRAMS PER DAY, AND OFTEN INVOLVE MORE THAN ONE ACETAMINOPHEN-CONTAINING PRODUCT.

CONTRAINDICATIONS

VICODIN, VICODIN ES, and VICODIN HP tablets are contraindicated in patients previously exhibiting hypersensitivity to hydrocodone or acetaminophen, and also in patients known to be hypersensitive to other opioids, as they may exhibit cross-sensitivity to hydrocodone.

WARNINGS

Controlled Substance: VICODIN, VICODIN ES, and VICODIN HP contain hydrocodone, which is an opioid agonist and a Schedule III controlled substance with an abuse liability.

Abuse and Dependence: VICODIN, VICODIN ES, and VICODIN HP can be abused in a manner similar to other opioid agonists, legal or illicit. Psychological dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, these products should be prescribed and administered with caution.

Hypersensitivity/Anaphylaxis: There have been post-marketing reports of hypersensitivity and anaphylaxis associated with use of acetaminophen.

Respiratory Depression: At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression.

Head Injury and Increased Intracranial Pressure: The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury or other intracranial pressure.

Acute Abdominal Conditions: The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

PRECAUTIONS

As with any narcotic, special caution should be used when prescribing hydrocodone to elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy, or urethral stricture. Caution should also be exercised with patients who are likely to take other acetaminophen-containing medications, antihistamines, antipsychotics, antianxiety agents, other narcotic analgesics, or other central nervous system (CNS) depressants (including alcohol) concomitantly. When combined therapy is contemplated, the dose of one or both agents should be reduced. Hydrocodone, like all narcotics, may impair mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a car or operating machinery.

(continued on next page)

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The use of monoamine oxidase (MAO) inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone.

VICODIN, VICODIN ES, and VICODIN HP tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. Administration to the mother during labor or shortly before delivery may result in some degree of respiratory depression in the newborn.

ADVERSE REACTIONS

The most frequently reported adverse reactions include lightheadedness, dizziness, sedation, nausea, and vomiting. Prolonged administration may produce constipation.

DOSAGE AND ADMINISTRATION

- **VICODIN 5 mg/300 mg:** The usual adult dosage is one or two tablets every four to six hours as needed for pain. The total daily dosage should **not exceed 8 tablets**.
- **VICODIN ES 7.5 mg/300 mg:** The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dosage should **not exceed 6 tablets**.
- **VICODIN HP 10 mg/300 mg:** The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dosage should **not exceed 6 tablets**.

DOSAGE AND ADMINISTRATION

- **VICODIN 5 mg/500 mg:** The usual adult dosage is one or two tablets every four to six hours as needed for pain. The total daily dosage should **not exceed 8 tablets**.
- **VICODIN ES 7.5 mg/750 mg:** The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dosage should **not exceed 5 tablets**.
- **VICODIN HP 10 mg/660 mg:** The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dosage should **not exceed 6 tablets**.

Sincerely,

Michael A. Jones
Divisional Vice President and
General Manager, Mature Businesses
MAJ/aab

Please see accompanying Full Prescribing Information.

References: 1. VICODIN, VICODIN ES, VICODIN HP 5, 7.5, 10 mg (hydrocodone)/300 mg (acetaminophen) [package insert]. **2.** United States Department of Health and Human Services. FDA drug safety communication. Food and Drug Administration Web site. http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm. Accessed June 13, 2013. **3.** Data on file, AbbVie Inc. **4.** U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Approved Drug Products with Therapeutic Equivalence Evaluations. 32nd ed. http://www.fda.gov/downloads/Drugs/DevlopmentApprovalProcess/UCM071436.pdf. Accessed January 14, 2013. **5.** VICODIN 5 mg (hydrocodone)/500 mg (acetaminophen) [package insert]. **6.** VICODIN ES 7.5 mg (hydrocodone)/750 mg (acetaminophen) [package insert]. **7.** VICODIN HP 10 mg (hydrocodone)/660 mg (acetaminophen) [package insert].

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