



## 2013 Consumer Safety Update: FDA Safety

Throughout the year, the U.S. Food and Drug Administration issues safety communications for products and devices whose safety and integrity have come into question. PHP takes immediate action to inform members and providers when claims analysis indicates these issues directly or potentially affect the Plan member. These are reviewed at the Plan Pharmacy & Therapeutics Committee. The most recent FDA safety communications are provided here for reference in your practice. More information here: <http://www.fda.gov/>.



### November 25, 2013

**Drug Information Update.** FDA requires removal of some prescribing and dispensing restrictions for rosiglitazone-containing diabetes medicine.

**ISSUE:** FDA has determined that recent data for rosiglitazone-containing drugs, such as Avandia, Avandamet, Avandaryl, and generics, do not show an increased risk of heart attack compared to the standard type 2 diabetes medicines metformin and sulfonylurea. As a result, FDA is requiring removal of the prescribing and dispensing restrictions for rosiglitazone medicines that were put in place in 2010. This decision is based on FDA review of data from a large, long-term clinical trial and is supported by a comprehensive, outside, expert re-evaluation of the data conducted by the Duke Clinical Research Institute (DCRI). Previous data from a large, combined analysis of mostly short-term, randomized clinical trials of rosiglitazone had suggested an elevated risk of heart attack, so FDA required a Risk Evaluation and Mitigation Strategy (REMS), called the Rosiglitazone REMS program. The Rosiglitazone REMS program restricted the use of rosiglitazone medicines to help ensure that their benefits outweighed the risks. Although some scientific uncertainty about the cardiovascular safety of rosiglitazone medicines still remains, in light of the new re-evaluation of the Rosiglitazone Evaluated for Cardiovascular Outcomes and Regulation of Glycemia in Diabetes (RECORD) trial, FDA's concern is substantially reduced and the rosiglitazone REMS program requirements will be modified.

**RECOMMENDATION:** Patients with type 2 diabetes should continue to work closely with their health care professionals to determine treatment options that are most appropriate. Health care professionals, pharmacies, and patients will no longer be required to enroll in the rosiglitazone REMS program to be able to prescribe, dispense, or receive rosiglitazone medicines.

### November 13, 2013

**Over-the-Counter Topical Antiseptic Products.** FDA Requests Label Changes and Single-Use Packaging to Decrease Risk of Infection

**ISSUE:** The U.S. Food and Drug Administration (FDA) is requesting label and packaging changes to enhance the safe use of certain over-the-counter (OTC) topical antiseptic products. This request is the result of our ongoing evaluation of infrequent but continuing reports of infections resulting from antiseptic products labeled for preoperative or preinjection skin preparation.

**RECOMMENDATION:** To further reduce the risk of infection with improper topical antiseptic use and the possibility of these products becoming contaminated with bacteria during use, we are requesting that manufacturers package antiseptics indicated for preoperative or preinjection skin preparation in single-use containers.

**No Plan Action - OTC**

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**November 20, 2013**

**Drug Information Update.** FDA warns of rare but serious risk of heart attack and death with cardiac nuclear stress test drugs Lexiscan (regadenoson) and Adenoscan (adenosine)

The U.S. Food and Drug Administration (FDA) is warning health care professionals of the rare but serious risk of heart attack and death with use of the cardiac nuclear stress test agents Lexiscan (regadenoson) and Adenoscan (adenosine). We have approved changes to the drug labels to reflect these serious events and updated our recommendations for use of these agents. Health care professionals should avoid using these drugs in patients with signs or symptoms of unstable angina or cardiovascular instability, as these patients may be at greater risk for serious cardiovascular adverse reactions.

**No Plan Action – Medical**

**November 14, 2013**

**Drug Information Update.** FDA warns about counterfeit ExtenZe dietary supplements

The U.S. Food and Drug Administration is warning consumers about a potentially harmful counterfeit dietary supplement for male sexual enhancement, represented as “ExtenZe Maximum Strength.” The counterfeit product looks similar to the actual product, but can be identified by lot number 0512058 and the expiration date EXP. May 16 stamped on the outer carton and embossed on the blister card. FDA laboratory analysis confirmed that the counterfeit ExtenZe product contains sildenafil, an active ingredient in FDA-approved prescription medicines for erectile dysfunction. This undeclared ingredient may interact with nitrates found in some prescription drugs, such as nitroglycerin, and may lower blood pressure to dangerous levels. Men with diabetes, high blood pressure, high cholesterol, or heart disease often take nitrates.

**No Plan Action - OTC**

**November 6, 2013**

**Low Molecular Weight Heparins.** Recommendations to Decrease Risk of Spinal Column Bleeding and Paralysis

**ISSUE:** The U.S. Food and Drug Administration (FDA) is recommending that health care professionals carefully consider the timing of spinal catheter placement and removal in patients taking anticoagulant drugs, such as enoxaparin, and delay dosing of anticoagulant medications for some time interval after catheter removal to decrease the risk of spinal column bleeding and subsequent paralysis after spinal injections, including epidural procedures and lumbar punctures. These new timing recommendations, which can decrease the risk of epidural or spinal hematoma, will be added to the labels of anticoagulant drugs known as low molecular weight heparins, including Lovenox and generic enoxaparin products and similar products.

**No Plan Action – Hospital**

**November 6, 2013**

**Drug Information Update.** UPDATE to FDA Drug Safety Communication: FDA asks manufacturer of the leukemia drug Iclusig (ponatinib) to suspend marketing and sales.

**No Plan Action - No claims**

**October 31, 2013**

**FDA Drug Safety Communication.** FDA asks manufacturer of the leukemia drug Iclusig (ponatinib) to suspend marketing and sales

The U.S. Food and Drug Administration (FDA) has asked the manufacturer of the leukemia chemotherapy drug Iclusig (ponatinib) to suspend marketing and sales of Iclusig because of the risk of life-threatening blood clots and severe narrowing of blood vessels.

**No claims**

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### October 25, 2013

**Drug Information Update.** FDA approves extended-release, single-entity hydrocodone product  
The U.S. Food and Drug Administration today approved Zohydro ER (hydrocodone bitartrate extended-release capsules) for the management of pain severe enough to require daily, around-the-clock, long-term treatment and for which alternative treatment options are inadequate. Zohydro ER, a Schedule II controlled substance under the Controlled Substances Act, is the first FDA-approved single-entity (not combined with an analgesic such as acetaminophen) and extended-release hydrocodone product

### October 25, 2013

**Drug Information Update.** Proposed Hydrocodone Reclassification  
In 2009, the U.S. Drug Enforcement Administration (DEA) asked the U.S. Department of Health and Human Services (HHS) for a recommendation regarding whether to change the schedule for hydrocodone combination products, such as Vicodin. The proposed change was from Schedule III to Schedule II, which would increase the controls on these products. *Due to the unique history of this issue and the tremendous amount of public interest, we are announcing the agency's intent to recommend to HHS that hydrocodone combination products should be reclassified to a different and more restrictive schedule.*

### October 11, 2013

**Drug Safety Communication.** Iclusig (Ponatinib) Increased Reports Of Serious Blood Clots In Arteries And Veins

**ISSUE:** FDA is investigating an increasing frequency of reports of serious and life-threatening blood clots and severe narrowing of blood vessels (arteries and veins) of patients taking the leukemia chemotherapy drug Iclusig (ponatinib).

**BACKGROUND:** Iclusig is a prescription medicine used to treat adults diagnosed with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL), who are no longer benefiting from previous treatment or who did not tolerate other treatment. At the time of Iclusig's approval in December 2012, the drug label contained information about the risks of blood clots in the Boxed Warning and Warnings and Precautions sections. In clinical trials conducted before approval, serious arterial blood clots occurred in 8 percent of Iclusig-treated patients, and blood clots in the veins occurred in 3 percent of Iclusig-treated patients. In the most recent clinical trial data submitted by the manufacturer to FDA, at least 20 percent of all participants treated with Iclusig have developed blood clots or narrowing of blood vessels.

### October 8, 2013

#### Health Advisory

OxyElite Pro-Acute Hepatitis Illness Cases Linked to Product Use

**ISSUE:** The FDA, along with the Centers for Disease Control and Prevention (CDC) and the Hawaii Department of Health (DOH), are investigating a growing number of reports of acute non-viral hepatitis in Hawaii. The Hawaii DOH has reported that 24 of these cases share a common link to a dietary supplement product labeled as OxyElite Pro. There have been 29 cases of acute non-viral hepatitis with an unknown cause identified in the state of Hawaii. Eleven of the 29 cases have been hospitalized with acute hepatitis, two cases have received liver transplants and one person has died. CDC is also looking at other cases of liver injury nationwide that may be related.

### 09/27/2013

**Drug Safety Communication.** Tygacil (tigecycline): Increased Risk of Death

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**Drug Information Update :** FDA Drug Safety Communication: FDA warns of increased risk of death with IV antibacterial Tygacil (tigecycline) and approves new Boxed Warning. This analysis showed a higher risk of death among patients receiving Tygacil compared to other antibacterial drugs: 2.5% (66/2640) vs. 1.8% (48/2628), respectively. The adjusted risk difference for death was 0.6% with corresponding 95% confidence interval (0.0%, 1.2%). In general, the deaths resulted from worsening infections, complications of infection, or other underlying medical conditions. Health care professionals should reserve Tygacil for use in situations when alternative treatments are not suitable. Tygacil is FDA-approved to treat complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI), and community-acquired bacterial pneumonia (CABP).

**No claims**

**September 25, 2013**

**Drug Safety Communication.** Arzerra (ofatumumab) and Rituxan (rituximab): New Boxed Warning, Recommendations to Decrease Risk of Hepatitis B Reactivation

The U.S. Food and Drug Administration (FDA) has approved changes to the prescribing information of the immune-suppressing and anti-cancer drugs Arzerra (ofatumumab) and Rituxan (rituximab) to add new Boxed Warning information about the risk of reactivation of hepatitis B virus (HBV) infection. In patients with prior HBV infection, HBV reactivation may occur when the body's immune system is impaired.

**Reviewed with Medical Directors – No Plan Action recommended**

**September 23, 2013**

**Drug Safety Communication.** Duragesic (fentanyl) Patches: Packaging Changes to Minimize Risk of Accidental Exposure

FDA is requiring color changes to the writing on Duragesic (fentanyl) pain patches so they can be seen more easily. FDA continues to learn of deaths from accidental exposure to fentanyl patches. In an effort to minimize the risk of accidental exposure to fentanyl patches, FDA is requiring the manufacturer of Duragesic to print the name and strength of the drug on the patch in long-lasting ink, in a color that is clearly visible to patients and caregivers. The current ink color varies by strength and is not always easy to see. This change is intended to enable patients and caregivers to more easily find patches on patients' bodies and see patches that have fallen off, which children or pets could accidentally touch or ingest. The manufacturers of generic fentanyl patches are being requested to make similar changes.

**Reviewed with Medical Directors – No Plan Action recommended**

**September 16, 2013**

**Drug Information Update.** FDA prohibits manufacture of FDA-regulated drugs from Ranbaxy's Mohali, India, plant and issues import alert.

The U.S. Food and Drug Administration today issued an import alert under which U.S. officials may detain at the U.S. border drug products manufactured at Ranbaxy Laboratories, Ltd.'s facility in Mohali, India. The firm will remain on the import alert until the company complies with U.S. drug manufacturing requirements, known as current good manufacturing practices (CGMP).

**September 10, 2103**

**Drug Information Update.** FDA announces safety labeling changes and postmarket study requirements for extended-release and long-acting opioid analgesics.

The U.S. Food and Drug Administration today announced class-wide safety labeling changes and new postmarket study requirements for all extended-release and long-acting (ER/LA) opioid analgesics intended to treat pain. Given the serious risks of using ER/LA opioids, the class-wide labeling changes, when final, will include important new language to help health care professionals tailor their prescribing decisions based on a

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patient's individual needs. The updated indication states that ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

**August 29, 2013**

**Drug Safety Communication.** FDA investigating rare brain infection in patient taking Gilenya (fingolimod) The U.S. Food and Drug Administration (FDA) is alerting the public that a patient in Europe diagnosed with possible multiple sclerosis (MS) has developed a rare and serious brain infection after taking the drug Gilenya (fingolimod). This is the first case of this disease, called progressive multifocal leukoencephalopathy or PML, reported following the administration of Gilenya to a patient who had not previously received Tysabri (natalizumab), an MS drug associated with a higher risk of PML

**August 15, 2013**

**FDA Drug Safety Communication:** FDA requires label changes to warn of risk for possibly permanent nerve damage from antibacterial fluoroquinolone drugs taken by mouth or by injection. The U.S. Food and Drug Administration (FDA) has required the drug labels and Medication Guides for all fluoroquinolone antibacterial drugs be updated to better describe the serious side effect of peripheral neuropathy. This serious nerve damage potentially caused by fluoroquinolones may occur soon after these drugs are taken and may be permanent. The risk of peripheral neuropathy occurs only with fluoroquinolones that are taken by mouth or by injection. Approved fluoroquinolone drugs include levofloxacin (Levaquin), ciprofloxacin (Cipro), moxifloxacin (Avelox), norfloxacin (Noroxin), ofloxacin (Floxin), and gemifloxacin (Factive). The topical formulations of fluoroquinolones, applied to the ears or eyes, are not known to be associated with this risk.

**August 6, 2013**

**Drug Information Update.** New Federal Guidelines for Managing Occupational Exposures to HIV New guidelines from the United States Public Health Service update the recommendations for the management of healthcare personnel (HCP) with occupational exposure to HIV and use of post-exposure prophylaxis (PEP). The guidelines, published online today in Infection Control and Hospital Epidemiology, the journal of the Society for Healthcare Epidemiology of America (SHEA), emphasize the immediate use of a PEP regimen containing three or more antiretroviral drugs after any occupational exposure to HIV. The PEP regimens recommended in the guidelines encourage the consistent use of a combination of three or more drugs, that are better tolerated than those recommended in the previously published guidelines from 2005, for all occupational exposures to HIV. The guidance eliminates the previous recommendation to assess the level of risk associated with individual exposures to help determine the appropriate number of drugs recommended for PEP.

**August 1, 2013**

**Drug Information Update.** FDA warns of rare but serious skin reactions with the pain reliever/fever reducer acetaminophen. The U.S. Food and Drug Administration (FDA) is informing the public that acetaminophen has been associated with a risk of rare but serious skin reactions. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. Acetaminophen is a common active ingredient to treat pain and reduce fever; it is included in many prescription and over-the-counter (OTC) products.

**May 30, 2013**

**Drug Safety Communication**

Magnesium Sulfate: - Recommendation Against Prolonged Use in Pre-term Labor

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FDA is advising health care professionals against using magnesium sulfate injection for more than 5-7 days to stop pre-term labor in pregnant women. Administration of magnesium sulfate injection to pregnant women longer than 5-7 days may lead to low calcium levels and bone problems in the developing baby or fetus, including thin bones (osteopenia), and fractures.

**May 14, 2013**

**Drug Safety Communication:**

FDA approves label changes for zolpidem products, including new dosing and a recommendation to avoid driving the day after Ambien CR use

FDA is also warning that patients who take the sleep medication zolpidem extended-release (Ambien CR)—either 6.25 mg or 12.5 mg—should not drive or engage in other activities that require complete mental alertness the day after taking the drug because zolpidem levels can remain high enough the next day to impair these activities.

**May 6, 2013**

**Drug Safety Communication**

Kadcyla (ado-trastuzumab emtansine): - Potential Medication Errors Resulting from Name Confusion

The FDA notified health care professionals that the use of the incorrect nonproprietary name for the breast cancer drug Kadcyla (ado-trastuzumab emtansine) in some medication-related electronic systems poses a risk of mix-up with Herceptin (trastuzumab) and may result in medication errors. The dosing and treatment schedules for Kadcyla and Herceptin, another breast cancer drug, are quite different, so confusion between these products could lead to dosing errors and potential harm to patients.

The FDA-approved nonproprietary name for Kadcyla, ado-trastuzumab emtansine, should be used. However, some third-party publications, compendia references, health information systems (e.g., electronic health record systems and systems used for pharmacy prescription processing, wholesaler ordering, pharmacy ordering, etc.), and sites on the Internet are incorrectly using the United States Adopted Name (USAN), which is "trastuzumab emtansine," and omitting the "ado" prefix and hyphen. Use of this truncated version of Kadcyla's nonproprietary name may cause confusion with Herceptin (trastuzumab).

**May 6, 2013**

**FDA Drug Safety Communication**

Valproate Anti-seizure Products Contraindicated for Migraine Prevention in Pregnant Women due to Decreased IQ Scores in Exposed Children

Stronger warnings about use during pregnancy will be added to the drug labels, and valproate's pregnancy category for migraine use will be changed from "D" (the potential benefit of the drug in pregnant women may be acceptable despite its potential risks) to "X" (the risk of use in pregnant women clearly outweighs any possible benefit of the drug).

With regard to valproate use in pregnant women with epilepsy or bipolar disorder, valproate products should only be prescribed if other medications are not effective in treating the condition or are otherwise unacceptable. Valproate products will remain in pregnancy category D for treating epilepsy and manic episodes associated with bipolar disorder.

With regard to women of childbearing age who are not pregnant, valproate should not be taken for any condition unless the drug is essential to the management of the woman's medical condition. All non-pregnant women of childbearing age taking valproate products should use effective birth control.

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**April 26, 2013**

**Drug Safety Communication**

Potiga (Ezogabine): - Linked To Retinal Abnormalities And Blue Skin Discoloration

Potiga (Ezogabine): Drug Safety Communication - Linked To Retinal Abnormalities And Blue Skin Discoloration

ISSUE: FDA is warning the public that the anti-seizure medication Potiga (Ezogabine) can cause blue skin discoloration and eye abnormalities characterized by pigment changes in the retina. FDA does not currently know if these changes are reversible. FDA is working with the manufacturer to gather and evaluate all available information to better understand these events. FDA will update the public when more information is available

**No action by Plan – Zero claims**

**April 17, 2013**

**Drug Information Update**

FDA approves abuse-deterrent labeling for reformulated OxyContin (Agency will not approve generics to original OxyContin)