The Pharmacist Activist

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Editorial

CVS – Criminal Charges are Needed!

On October 14, 2010, the U. S. Drug Enforcement Administration (DEA) issued a news release titled, "CVS to Pay Largest Ever Civil Penalty Under Controlled Substances Act." The following statements are among those included in the news release:

> "In an agreement finalized late yesterday, CVS Pharmacy, Inc., the biggest operator of retail pharmacies in the United States, has admitted that it unlawfully sold pseudoephedrine to criminals who made methamphetamine. As part of the agreement with federal prosecutors, CVS has agreed to pay $75 million in civil penalties and to forfeit the $2.6 million in profits the company earned as a result of the illegal conduct."
>
> "CVS's flagrant violation of the law resulted in the company becoming a direct link in the methamphetamine supply chain."
>
> "As part of the agreement, the government has agreed not to pursue criminal charges against CVS, which has accepted responsibility for the illegal conduct and has agreed to implement a compliance and ethics program over the next three years."

(For a more detailed discussion of this situation, please see my editorial, "Strike 3 –CVS Should be OUT!" in the November 2010 issue of *The Pharmacist Activist* at www.pharmacistactivist.com).

It is impossible to know how much harm and how many deaths resulted from the methamphetamine abuse that was enabled by the illegal conduct of CVS in selling huge amounts of pseudoephedrine, but there must have been numerous tragic consequences. However, the DEA also made a mistake – *it should have pursued criminal charges against CVS*. Why would criminal charges not be pursued when there was illegal conduct that placed many individuals at risk of harm and death? The lack of such action invites the question as to whether there is a monetary threshold ($75 million?) at which criminal charges can be avoided. Regrettably, the payment of a $75 million fine has not been a

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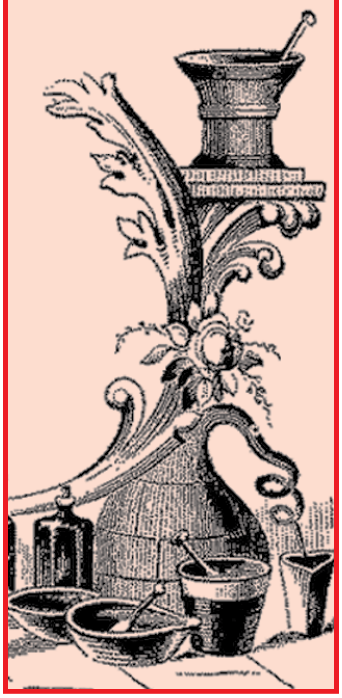

sufficient deterrent to prevent certain CVS stores from selling large amounts of other agents of abuse, or cause for CVS management to implement effective precautions and monitoring controls.

Oxycodone

The widespread abuse of oxycodone and the resultant problems are well recognized. According to the Centers for Disease Control and Prevention, the number of deaths each year attributed to painkillers has quadrupled in the last decade to nearly 15,000, and surpass those from heroin and cocaine combined. Earlier this month, the DEA moved to suspend two CVS pharmacies in Sanford, Florida and the Cardinal Health facility in Lakeland, Florida from selling controlled substances. This action was based on concerns regarding the very large amounts of oxycodone that were being sold by these companies. This situation has received extensive news coverage including two detailed articles in the *Wall Street Journal* written by Devlin Barrett and Timothy Martin ("Pharmacies Swept Into Drug Wars", February 15, 2012, page B1; "Red Flags Ignored, DEA Says", February 21, 2012, page B1)*.

The observations and allegations of the DEA regarding the two CVS pharmacies include the following:

- They were dispensing "staggering" amounts of oxycodone.
- The two pharmacies purchased approximately 3 million oxycodone tablets in a year (compared with approximately 69,000 tablets a year in an average pharmacy).
- One of the CVS stores reported that 58% of the prescriptions for oxycodone were paid for in cash (compared with the approximately 7% rate at which all prescriptions nationwide are paid for in cash).
- Approximately every third car through the drive-through lane had prescriptions for oxycodone or hydrocodone.
- These pharmacies knew or should have known that a large number of these prescriptions were not issued for legitimate medical purposes.
- The pharmacies should have recognized misspelled drug names, irregular dosing instructions, and phony telephone numbers on prescriptions.
- The pharmacies are an "imminent danger" to the public.

The *Wall Street Journal* coverage includes the content of an internal Cardinal Health email attached to the DEA filing: "A CVS pharmacy corporate employee told the distributor that the rising purchase orders for oxycodone were no cause for alarm. Soaring demand for the painkiller, the CVS employee explained to Cardinal, stemmed from Florida authorities' crackdown on illicit suppliers, or 'pill mills,' leading to an increase in legitimate traffic at CVS."

CVS's response

Last fall I learned that CVS had informed some Florida physicians that it would no longer dispense their prescriptions for narcotics. I was impressed that CVS had taken this action. Now, however, I realize that CVS took this action only after it learned of the investigations being conducted by the DEA. The responses that CVS has provided regarding the DEA allegations include the following:

> "CVS/pharmacy is unwavering in its compliance with and support of the measures taken by federal and state law enforcement officials to prevent drug abuse and keep controlled substances out of the wrong hands."
>
> "Allegations regarding past conduct do not reflect the pharmacies' practices today."
>
> "We informed a small number of Florida physicians that CVS/pharmacy will no longer fill the prescriptions they write for Schedule II narcotics. Distributions of oxycodone to the two Florida stores have decreased by approximately 80% in the last three months compared to the prior three months – we believe in large part due to our action."

For CVS to try to take credit for a reduction in oxycodone purchases by its two pharmacies is blatant deception. These two pharmacies were *caught* purchasing and dispensing oxycodone in quantities that are far

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New Drug Review

Roflumilast
(Daliresp – Forest)

Agent for Chronic Obstructive Pulmonary Disease

New Drug Comparison Rating (NDCR) = 3

(no or minor advantages/ disadvantages) in a scale of 1 to 5 with 5 being the highest rating

Indication:
To reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.

Comparable drug:
Tiotropium (Spiriva).

Advantages:
- Has a unique mechanism of action (selective phosphodiesterase 4 inhibition);
- May increase the effectiveness of the COPD regimen;
- Is administered orally.

Disadvantages:
- Labeled indication is more limited (e.g., for patients with *severe* COPD associated with chronic bronchitis [but not emphysema]);
- Effectiveness is limited ("modest");
- Has not been directly compared with other drugs in clinical studies;
- Psychiatric adverse events (anxiety, depression, suicidal ideation) have been reported with its use;
- Is contraindicated in patients with moderate or severe hepatic impairment.

Most important risks/adverse events:
Contraindicated in patients with moderate or severe hepatic impairment; psychiatric adverse events (e.g., anxiety, depression, suicidal ideation; caution must be exercised in patients with a history of depression and/or suicidal thoughts or behavior); weight loss (weight should be regularly monitored); should not be used for the relief of acute bronchospasm; action may be increased by the concurrent use of a CYP3A4 or CYP1A2 inhibitor (e.g., ketoconazole, fluvoxamine), and decreased by the concurrent use of a CYP3A4 inducer (e.g., rifampin).

Most common adverse events:
Diarrhea (10%), weight loss (8%), nausea (5%), headache (4%), back pain (3%), insomnia (2%), dizziness (2%).

Usual dosage:
500 mcg once a day.

Product:
Tablets – 500 mcg.

Comments:
Chronic obstructive pulmonary disease (COPD) is often associated with chronic bronchitis or emphysema. A significant worsening of symptoms (i.e., exacerbations) may last for several weeks and be severe enough to require hospitalization. The medications used most often in the treatment of COPD include bronchodilators (e.g., beta-2 adrenergic receptor agonists [e.g., salmeterol (Serevent)], anticholinergic agents [tiotropium (Spiriva)]) and inhaled corticosteroids (used in combination with a beta-2 agonist [Advair, Symbicort]).

Roflumilast and its active metabolite (roflumilast N-oxide) are selective inhibitors of the enzyme phosphodiesterase 4 (PDE4). Inhibition of this enzyme results in an increase

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greater than can be explained by legitimate need. The action of CVS management occurred *after* it became aware of the DEA investigation, and appears to be motivated by protection of its corporate interests and not by concern for the individuals who obtained the large quantities of oxycodone from its pharmacies.

The DEA initiated action to suspend the two CVS pharmacies and two independent pharmacies from purchasing and dispensing controlled substances. The two independent pharmacies voluntarily surrendered their controlled substance licenses. The two CVS pharmacies went to court and obtained a temporary restraining order against the DEA's action although they have reportedly voluntarily stopped dispensing oxycodone.

Consequences

It is estimated that seven people die each day in Florida as a result of overdosage with prescription drugs. How many of these deaths during the last several years can be attributed to the huge amounts of oxycodone that were sold by these two CVS pharmacies? The fast answer is that we don't know. However, the investigation must be continued. It can be anticipated that some "patients" will have died, some will be impossible to locate, some will have a legitimate need for oxycodone, and others will not. Some drug-related problems, including deaths, never become known to the DEA, other regulatory agencies, or the police, but do become the subject of litigation. Typically, these lawsuits are settled out of court without an acknowledgement of wrongdoing and with the terms of the settlement considered confidential. The investigation of CVS should include an examination of the lawsuits regarding drug-related problems and alleged errors or negligence that have been initiated against the company. If inappropriate actions and/or negligence persist that place individuals' lives at risk, criminal charges should be pursued and the entire company should not be permitted to purchase and dispense controlled substances.

Daniel A. Hussar

*As this issue of *The Pharmacist Activist* was going to press, another detailed account of the DEA actions in Florida was published as the cover story in *USA Today* ("DEA aims big to stem painkiller black market", by Donna Leger, February 28, 2012, page 1A).

New Drug Review (cont.)

of intracellular cyclic AMP in lung cells and a reduction in inflammation. Roflumilast is indicated for use in patients with severe COPD associated with chronic bronchitis. It has not been evaluated for the treatment of COPD associated with emphysema. Its effectiveness was demonstrated in multiple studies including two one-year trials. There was a significant reduction in the rate of moderate or severe exacerbations in those treated with roflumilast compared to placebo, with a 15% reduction in exacerbations in one trial and an 18% reduction in the other. This benefit has been viewed by some as "modest" and, in the context of a potential for systemic adverse events, its labeled indication limits its use to patients with severe COPD.

Roflumilast is converted to its active metabolite primarily via the CYP3A4 and CYP1A2 pathways. Although the parent drug is three times as potent as its metabolite, the plasma exposure of the metabolite is about 10-fold greater.

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