



ISMP

Medication Safety Alert!®

Community/Ambulatory Care Edition

Educating the Healthcare Community
About Safe Medication Practices



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Little patches...Big problems. New safety warnings about fentanyl patches - Part 1

The FDA is conducting an investigation into reports of serious side effects including death due to overdoses of fentanyl in patients using fentanyl transdermal patches for pain control. We urge everyone who prescribes, dispenses, or administers fentanyl patches (both **DURAGESIC** and generic brands) to thoroughly review the recent FDA Public Health Advisory and an alert from Janssen about updated safety information that has been added to the product labeling (links can be found at www.ismp.org/MSAarticles/fdasafetyalerts.htm). As noted by FDA, some patients, as well as their healthcare providers, may not be completely aware of the dangers of these products and the important recommendations regarding their safe use. ISMP considers fentanyl a high-alert medication, which means that it is not necessarily more prone to errors, but if used in error, there is a greater risk of patient harm or death.

ISMP and other patient safety advocates have long been concerned that transdermal fentanyl is often prescribed and dispensed without proper consideration of patient selection criteria, starting dose recommendations, contraindications, dose adjustment recommendations, and safe administration procedures. However, our concern was heightened just days before the FDA and Janssen releases when we heard from a nurse practitioner who shared a report about the recent death of a family member who was using fentanyl patches. In this article we will share information about the various types of errors that have been reported to the USP-ISMP Medication Errors Reporting Program (MERP) and the FDA MedWatch program involving fentanyl patches. We will also highlight portions of the Janssen alert and the FDA Advisory that are pertinent to these errors.

“Off-label” use of fentanyl patches has led to patient harm, including the recent death mentioned above. In this case, a 77-year-old woman died in March due to misprescribing, inadequate patient education, and subsequent confusion about how to use a fentanyl patch. One week prior to her death, she was given a prescription for **VICODIN** (hydrocodone and acetaminophen) 5 mg/500 mg QID for sciatic pain. She took about 4 doses daily for a week, but *cont'd on page 2*

Safety Briefs

■ **Coumadin – Cardura mix-ups.** A long-term care pharmacy received the following faxed copy of a handwritten order for **CARDURA** (doxazosin) 1 mg HS. The order was misinterpreted and dispensed as **COUMADIN** (warfarin) 1 mg HS. Subsequently, the patient received 20 doses of Coumadin instead of



Cardura before the error was discovered during a hospitalization for uncontrolled hypertension. In another report, a prescription for Cardura 2 mg was incorrectly entered into the pharmacy computer as Coumadin 2 mg, but Cardura was correctly selected from pharmacy stock and placed into the vial. Unfortunately, due to the initial processing error, the prescription was refilled twice with Coumadin before the error was detected.

Both of these medications are available in 1 mg, 2 mg, and 4 mg tablets, and are generally administered once daily. In addition, the names may look similar when poorly handwritten. To avoid mix-ups with these and other commonly confused drug name pairs, alert staff and other healthcare practitioners about these examples of errors. Physicians should be encouraged to include the medication's purpose on all prescriptions. Likewise, pharmacists and nurses should verify a medication's purpose (with the patient or prescriber) before it is dispensed or administered, especially for a high-alert medication such as warfarin. For commonly confused name pairs, consider adding alerts in the pharmacy and physician computer order entry systems. All practitioners must educate patients about their medications, so they are completely familiar with each product's name (brand and generic), purpose, and expected appearance.

■ **Confusion over newly marketed medications.** A pharmacist reported a potential error involving confusion between **INSPIRA** (eplerenone), a selective aldosterone receptor antagonist, and **SPIRIVA** *cont'd on page 2*

Fentanyl patches (cont'd from previous page)

was still in pain. She contacted her primary care physician who, by telephone, prescribed fentanyl 50 mcg per hour patches to be applied every 48-72 hours. A friend obtained the prescription from the pharmacy and was given a box of 5 patches (despite this state's law that allows only a 5-day supply of a phoned-in schedule II drug). The pharmacist did not provide education regarding proper use of the patch to either the friend or the patient. Not understanding how the patch provided pain relief, the woman's friend helped her place one of the patches on the site of her pain, the buttock. When the woman went to bed she used a heating pad on her lower back/buttock area, as was her usual practice. After 2 days of not hearing from the woman, friends went into her apartment and found her dead in bed. There were only 3 fentanyl patches left in the box so, although unconfirmed, it is suspected that a second patch may also have been applied.

Several errors contributed to this fatal outcome. First, the woman was not an appropriate candidate for a fentanyl patch. Product labeling states that these patches should only be used in patients who are already receiving opioid therapy, who have demonstrated opioid tolerance, and who require a total daily dose at least equivalent to a 25 mcg per hour fentanyl patch. Patients who are considered opioid-tolerant are those who have been taking at least 60 mg of oral morphine daily, 30 mg of oral oxycodone daily, or 8 mg of oral HYDROMORPHONE daily (or an equianalgesic dose of another opioid) for a week or longer. Use in non-tolerant patients, such as this one, has led to death from respiratory depression. A chart is available in the prescribing information to convert daily doses of opioids (of which hydrocodone is not included) to an appropriate starting dose of a fentanyl patch (see page 3 for this chart). In this case, the physician did not examine the patient, did not provide education to the patient about the drug and its potential side effects, and prescribed fentanyl over the phone.

Compounding the improper patient selection and the higher than recommended starting dose, the prescribed 48-hour dosing interval was inappropriate for this patient. The 48-hour dosing interval is to be reserved for patients who do not achieve adequate analgesia on the 72-hour regimen; a dose increase should be considered before adjusting the dosing interval. Unfortunately, the pharmacist did not question the initiation of fentanyl therapy, the strength prescribed, the dosing interval, and did not provide counseling. Also, neither practitioner warned the patient or her friend to avoid applying heat over the patch. Patients who experience an increase in body temperature or are exposed

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Safety Briefs (cont'd from previous page)

(tiotropium), an inhalation powder indicated for bronchospasm associated with COPD, including chronic bronchitis and emphysema. A physician ordered Spiriva 25 mg PO daily. Knowing that Spiriva is a powder for inhalation and shouldn't be swallowed, the pharmacist called the physician who verified that he confused the newer products and meant to write for Inspra 25 mg PO daily.

Product confusion was also reported between **SYMBYAX** (olanzapine and fluoxetine), used in the treatment of bipolar disorder, and **CYMBALTA** (duloxetine), used to manage diabetic neuropathic pain as well as depressive disorders. In this report, a physician prescribed Cymbalta for neuropathic pain; however, the pharmacist accidentally selected a Symbyax product from the pharmacy shelf. He realized his confusion when he saw that the selected medication was a combination product and not available in the prescribed 30 mg strength.

■ **Misunderstood abbreviations.** A physician prescribed "Amoxicillin 200 mg/5 mL" with instructions to administer 5 mL TID for a 3-year-old child. The pharmacy carried only a 250 mg/5 mL strength, so the pharmacist changed the directions to "Take 4 cc (4/5 teaspoonful) by mouth 3 times a day." The child's father misunderstood the directions, as English was his second language. He didn't know what "cc" meant, but upon seeing "4/5 teaspoonful," he thought he should give his child 4.5 teaspoons of the medication. After 5 doses, he brought his child to the emergency department with severe diarrhea. The use of two abbreviations contributed to the error: "cc" and a slash mark (/).

The child's father did not interpret either abbreviation as intended. Inadequate patient counseling also played a role. Although he had been given a 10 mL measuring device for oral solutions marked in mL and teaspoons, specific directions for measuring each dose were not reviewed with the father when picking up the prescription. Counseling is especially important if a pharmacist must use a different concentration of drug than originally prescribed, because the directions that the physician initially provides to the patient will differ from the actual directions on the prescription label.

Fentanyl patches (cont'd from previous page)

to external heat sources (e.g., heating pads, saunas, hot tubs, heated water beds) while using a patch may have a sudden and possibly dangerous increase in fentanyl absorption.

Fentanyl patches are indicated in the management of persistent, moderate to severe chronic pain that requires continuous, around-the-clock opioid administration for an extended period of time, and cannot be managed by other means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids. Due to the risk of serious or life-threatening hypoventilation, fentanyl patches are contraindicated in opioid-naïve patients, in the management of acute or postoperative pain, and in the management of mild or intermittent (e.g., prn) pain. However, healthcare practitioners who prescribe and dispense fentanyl patches may be unaware of, or overlook, these contraindications.

Unfortunately, Health Canada recently reported 2 cases of fentanyl patch use that resulted in adolescent deaths. In one case, a 15-year-old girl with chronic headaches was found unresponsive with respiratory depression 21 hours after the first patch was applied. She was resuscitated but suffered severe brain damage and died 2 days later. In the other case, a 14-year-old boy with throat pain due to mononucleosis was unable to be resuscitated after he was found in respiratory arrest 14 hours after the first patch was applied.

Prescribers must consider the prescribing information before initiating transdermal fentanyl therapy. Likewise, before dispensing or administering the medication, pharmacists and nurses must ensure that a fentanyl patch is indicated for the patient, that the dosage and dosing interval prescribed are appropriate for the patient, and that the patient and/or caregiver receives complete education regarding safe and proper use of the patch.

We have also received reports of errors due to improper titration of doses. In one case, a hospitalized opiate-tolerant patient was started at a 50 mcg per hour dosage; however, the dose was adjusted twice within 72 hours before the patient was discharged on a 100 mcg per hour dosage. At home, he experienced somnolence and confusion, fell, and was readmitted to the hospital. Prescribing information states that, after the initial patch application, evaluation of the maximum analgesic effect cannot be made until the patch is worn for at least 24 hours. The initial dose may be increased after 3 days based on the daily dose of supplemental opioid analgesics required by the patient in the second or third day after the initial application. After increasing the dose, it may take up to 6 days for the patient to reach equilibrium on the new dose. Therefore, patients should be

maintained at the increased dose through 2 applications before any further increase in dosage is made on the basis of the average daily use of a supplemental analgesic.

Look for additional safety issues and recommendations related to the use of fentanyl patches in Part 2 of this article in the September issue.

DOSE CONVERSION GUIDELINES¹

Current Analgesic	Daily Dosage (mg/d)			
	60-134	135-224	225-314	315-404
Oral morphine	60-134	135-224	225-314	315-404
IM/IV morphine	10-22	23-37	38-52	53-67
Oral oxycodone	30-67	67.5-112	112.5-157	157.5-202
IM/IV oxycodone	15-33	33.1-56	56.1-78	78.1-101
Oral codeine	150-447	448-747	748-1047	1048-1347
Oral hydromorphone	8-17	17.1-28	28.1-39	39.1-51
IV hydromorphone	1.5-3.4	3.5-5.6	5.7-7.9	8-10
IM meperidine	75-165	166-278	279-390	391-503
Oral methadone	20-44	45-74	75-104	105-134
IM methadone	10-22	23-37	38-52	53-67
Recommended DURAGESIC® Dose	25 mcg/h	50 mcg/h	75 mcg/h	100 mcg/h

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¹This table should not be used to convert from DURAGESIC® to other therapies because this conversion to DURAGESIC® is conservative. Use of this table for conversion to other analgesic therapies can overestimate the dose of the new agent. Overdosage of the new analgesic agent is possible (see dosage and administration - discontinuation of DURAGESIC®).

Share Your Stories with Us

Articles in this publication are based on actual reports from practitioners. We'd like to hear from you too! Please share



reports of medication errors and prevention recommendations, in confidence, with colleagues in the US and worldwide. Errors may be reported on the ISMP (www.ismp.org) or USP (www.usp.org) web sites or communicated directly to ISMP by calling 1-800-FAIL SAF(E) or through e-mail at ismpinfo@ismp.org. Reports are forwarded automatically to the FDA and to pharmaceutical companies whose products are mentioned in reports. Reporter identity and location are strictly confidential and never published. Be sure to visit our website for additional information.

Another acetaminophen error “drops” in

Last month we received a report about an 11-day-old infant whose parents were directed by their physician to administer **TYLENOL** (acetaminophen) Infants' Drops following his circumcision. A community pharmacist directed them to a store-brand equivalent product and instructed them to give the baby one-half dropperful for each dose. The pharmacist was familiar with the product, but did not realize that the manufacturer had recently changed the measuring device supplied with the product. It previously contained a dropper with a marking for “0.4 mL” and “0.8 mL” (see Figure 1), but the new package contained an oral syringe bearing only a “1.6 mL” mark nearly halfway up the syringe (see Figure 2). Subsequently, the infant received an unknown number of four-fold overdoses (intended dose was 40 mg [0.4 mL], baby received 160 mg [1.6 mL] per dose). The physician discovered the error when parents brought the baby in for follow up. The baby was hospitalized and treated with acetylcysteine for acetaminophen toxicity, but suffered no long-term harm.



Figure 1



Figure 2

While investigating this error, we learned that this product was part of a recent recall by Perrigo Company that involves several different formulations of concentrated infants' oral drops packaged with this poorly designed oral syringe. (A link to the FDA Alert can be found at www.ismp.org/MSAarticles/fdasafetyalerts.htm.) As illustrated in the case above, they are inappropriate for measuring doses less than 1.6 mL, which pediatricians may order for children less than 2 years of age.

However, this case illustrates a few other important points that should be considered. Practitioners must be fully aware of the over-the-counter products they recommend and keep in stock. To do so, manufacturers should provide an image of the device on the outer package. Then, pharmacists can see how dosages are indicated on the device and know its limitations. Also, because devices are available in different types (e.g., oral syringe, dropper), sizes, and with different markings, patients and

their caregivers must be provided with accurate dosing information for the specific product that is being used. For example, in this case, using the term “dropperful” was incorrect for the device provided, but it can also be misleading and may be misunderstood. However, if the parents were instructed to use 0.4 mL, they may have called to question how to administer the dose with the device provided. Similarly, it seems likely that the parents would have also overdosed their child with the previously available product since the

maximum fill line (0.8 mL) on the dropper is not even halfway up the pipette. Finally, practitioners must ensure that patients or their caregivers understand how to measure and administer the proper dose. This may require opening the package to provide a demonstration as well as a return demonstration by the patient or caregiver. Please share this report with your staff to illustrate the importance of communicating dosing information properly.

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The 2005 ISMP Cheers Awards: Looking for Medication Safety Stars

8th Annual ISMP Cheers Awards



Tuesday Evening, December 6, 2005

Join us at Cili Restaurant & Bar at the Bali Hai Golf Club, Las Vegas, NV
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This year's keynote speaker is **Billy Tauzin**, President and CEO,
Pharmaceutical Research and Manufacturers Association

Nominations Invited

The *ISMP Cheers Awards* are one of the most prestigious ways to recognize true leaders in the field of patient safety. They honor individuals, hospitals, health systems, or companies that have made extraordinary advances in medication safety in the past year. Nominations are also being accepted for the 2005 *ISMP Medication Safety Alert**! **Subscriber Award**, which honors an organization that widely distributes one or more of the ISMP newsletters (*Acute Care* edition, *Community/Ambulatory Care* edition, *Nurse Advise-ERR*[™], and *Safe Medicine*) and uses the information to improve medication safety.

Award recipients will be recognized for their outstanding contributions at the annual Cheers dinner banquet. They will receive an award, travel stipend to attend the banquet, and national recognition for their work.

Support Appreciated

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