Educating the healthcare community about safe medication practices
ISMP Medication Safety Alert! Acute Care

ONGOING, PREVENTABLE FATAL EVENTS WITH FENTANYL TRANSDERMAL PATCHES ARE ALARMING!

From the June 28, 2007 issue

Problem: Despite warnings from the FDA, manufacturers, and various patient safety agencies, fentanyl transdermal patches continue to be prescribed inappropriately to treat acute pain in opiate-naïve patients, sometimes in large doses or in combination with oral or intravenous opiates. Some of these prescribing errors have occurred in hospitals; others have originated in physician offices or ambulatory surgery centers, where well-meaning but misinformed primary care physicians or surgeons have prescribed the drug for opiate-naïve patients under contraindicated circumstances such as acute post-operative pain. Unfortunately, pharmacists have often filled these prescriptions without question, and nurses caring for patients have applied the patches without recognizing the prescribing error. ISMP is deeply troubled by these practices and alarmed by what appears to be a steady stream of reports of adverse events with fentanyl patches—including fatalities—caused by inappropriate prescribing, dispensing, and administration of the drug. The databases to which ISMP has access bear proof of this ongoing safety issue, and numerous case reports have already appeared in previous editions of ISMP newsletters (May 31, 2007; June 29, 2006; May 4, 2006; August 11, 2005; May 20, 2004; September 19, 2001).

As noted two years ago in our August 11, 2005 newsletter (*New fentanyl warnings: more needed to protect patients*), Ortho-McNeil (Janssen), maker of DURAGESIC (fentanyl transdermal), issued a "Dear Health Professional" letter to bring attention to new boxed warnings in the product label related to improper prescribing (www.fda.gov/medwatch/SAFETY/2005/duragesic_ddl.pdf). Likewise, FDA issued a Public Health Advisory (www.fda.gov/cder/drug/advisory/fentanyl.htm) to alert healthcare providers that deaths and overdoses had occurred in patients using both the brand name product Duragesic and the generic product. Despite these warnings, label changes, and publication of prescribing problems in ISMP newsletters and elsewhere, some practitioners still seem unaware of the dangers with this potent narcotic and the proper prescribing guidelines (see Table 1 at the end of the article).

In our May 31, 2007 newsletter, we reported that an elderly patient had several fentanyl patches totaling 125 mcg/hour applied to her skin, which caused delirium and led to her transfer to a critical care step-down unit for close observation. In the past few weeks, we received two more reports of prescribing errors—one of which was fatal.

In the first case, the person reporting the event described a post-operative patient with a morphine infusion running immediately after surgery, who was discharged the next day. According to the reporter, a nurse applied a prescribed fentanyl patch, 75 mcg/hour, to the patient's skin before discharge, and gave the patient three patches to take home as well as a prescription for oxycodone *prn* every 4-6 hours. Sadly, the patient died within 12 hours of discharge. We were told that the coroner attributed the patient's death to application of the fentanyl patch. Not only was this patient opiate naïve, and his pain not chronic, he was also being treated for sleep apnea and bronchopneumonia at the time of his surgery. Depending on its severity, existing respiratory compromise is another contra-indication to administering the drug.

In another event reported this month, an elderly patient was admitted to a hospital after application of a 100 mcg/hour patch to the skin. A family member had called the clinic where the patient had been receiving periodic epidural injections for back pain and asked a nurse to arrange an ambulance for transport for his next visit. This represented a significant change in the patient's status, so the nurse questioned the family and learned that a fentanyl patch had been prescribed, and that the patient had continued taking PERCOCET 5/325 (oxycodone 5 mg and acetaminophen 325 mg), two tablets, three or four times a day. After calling the patient's pharmacist to confirm his prescribed medications, the nurse called the family and told them to remove the patch immediately and take the patient to the emergency department (ED). The patient was admitted to the step-down unit. During the call to the patient's family, the nurse also confirmed that the patient and family had not been counseled when picking up the prescription. They had no awareness of the potency of the drug. Fortunately, this patient did not suffer any permanent adverse consequences.

Safe Practice Recommendations: The examples of errors described above are closely associated with a knowledge deficit about proper prescribing of fentanyl patches. These examples and others help substantiate the fact that reliance on product labeling and practitioner education alone will not do enough to solve this life-threatening problem. Yes, healthcare practitioners should be educated about safe prescribing, and the potency of fentanyl patches should be stressed. (You can view a free FDA Patient Safety Video [created in cooperation with ISMP] on this subject at: www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/transcript.cfm?show=44#2.) But there will always be those who are unaware of the great risks they take when prescribing fentanyl patches to opiate-naïve patients to treat acute pain.

Resources
Acute Care Main Page
Current Issue
Past Issues
Recent articles
Survey Results
Action Agendas - Free CEs
Special Error Alerts
Subscribe
Contest Winners
Newsletter Editions
Acute Care
Community/Ambulatory
Nursing
Consumer

Thus, prescribing guidelines along with checkpoints as described below must be established for this high-alert medication to help avoid the risk of patient harm.

Create guidelines. Specific prescribing and dispensing guidelines for fentanyl patches that are congruent with the product labeling should be developed and referenced during order entry of the medication in inpatient and outpatient settings. Fentanyl patches should only be used by patients who are opiate-tolerant with chronic pain that is not well controlled with shorter-acting analgesics. Equianalgesic conversion tables should also be included in the guidelines to help prescribers convert patients to an appropriate fentanyl transdermal dose based on preexisting opiate doses the patient has been taking.

Determine the indication. Pharmacists should determine the indication and ensure that the patient is opiate-tolerant and suffering from chronic pain before dispensing the medication. In inpatient settings, this information may come from the admission data set or nursing staff. In outpatient settings such as community pharmacies, the information must come from the patient profile, the prescriber, or from the patient (or patient's family) when the prescription is dropped off, ideally, or when providing counseling, if necessary. (See recommendation for mandatory counseling below.) If a new prescription is received for an opiate-naïve patient or the drug is intended to treat short-term pain, intermittent pain, or post-operative pain, the prescriber should be called to question the order. Verification of the indication and any conversations with the prescriber regarding the patient and the prescribed medication should be documented in a consistent place (e.g., pharmacy computer system, progress notes, order form, outpatient prescription).

Set dosing limits. The fentanyl patch should always be prescribed at the lowest dose needed for pain relief. Inpatient and outpatient pharmacy computer systems as well as computerized prescriber order entry systems should be designed to flash an alert on the screen and create a hard stop if more than 25 mcg/hour has been prescribed as a first-time dose. For patients who are admitted to the hospital and using fentanyl patches at home, the dose should be verified during medication reconciliation, and the verified drug list should be sent to the pharmacy. Healthcare providers should remain cautious about orders for a 125 mcg/hour strength because the decimal point has been overlooked at times with orders for 12.5 mcg/hour patches.

Assess concomitant use of opiates. To reduce the risk of an overdose, take into consideration any other opiates prescribed for the patient when evaluating the appropriateness of the patient's dose.

Limit prescribing privileges. In inpatient settings, consider limiting the prescribing of fentanyl patches to certain categories of prescribers who have been educated about the drug and privileged to prescribe it. Alternatively, orders for patches in doses greater than 25 mcg/hour could be limited to privileged prescribers, or the organization could require a review by a pain management specialist within a specified timeframe.

Mandatory patient education. Patients who are using a fentanyl patch and their caregivers should be educated about how to use the patch safely. In both inpatient and outpatient settings, this education should be mandatory and scripted for pharmacists and nurses to promote consistent discussions about: indications; potency; dose; safety precautions (e.g., avoid heating pads or hot tubs, remove old patch before application of a new patch); application, removal, and disposal processes; and signs of fentanyl toxicity. The patient package insert (or medication guide if one becomes available) should also be provided to the patient. In outpatient settings, pharmacists should use this counseling opportunity to verify that the patient is opiate-tolerant and being treated for ongoing chronic pain. All patient education should be documented in the patient record.

Know the signs of overdose. Healthcare practitioners who prescribe fentanyl patches, and nurses, patients, and caregivers who place the patches on the skin, should be aware of the signs of fentanyl overdoses, including: respiratory distress; shallow breathing; tiredness, extreme sleepiness, or sedation; inability to think, talk, or walk normally; and feeling faint, dizzy, or confused. If these signs occur, patients (or their caregivers) should seek medical attention immediately. Patients (and caregivers) should also know that they may have a sudden and possibly dangerous rise in their blood level of fentanyl or have a stronger effect from fentanyl if they: use other drugs that affect brain function; drink alcohol; have an increase in body temperature or are exposed to heat; or use other medications that affect how fentanyl is broken down in the body (e.g., ritonavir, ketoconazole).

ISMP has communicated with Ortho-McNeil and will also be contacting other manufacturers of fentanyl patches to alert them to the latest reports we have received about overdoses in opiate-naïve patients. We learned that Ortho-McNeil, maker of Duragesic, has filed an updated risk management plan for FDA approval that calls for ongoing surveillance to determine the scope of opiate-naïve patients who have been prescribed a fentanyl patch. They have also developed a patient medication guide, which healthcare providers will be required to give to patients, and indicated that the guide would be freely available on its website soon. We suggested that fentanyl transdermal sales forces provide targeted education to physician groups, perhaps standardizing the educational program and making it easily accessible to all healthcare practitioners. As an additional measure, ISMP will continue pursuing a collaborative effort with community pharmacy chains and independent pharmacies to further develop the mandatory education (counseling) process for patients, including scripted topics that detail the information that should be provided and documented.

Table 1. Excerpts from product labeling for fentanyl transdermal**

Indication
Fentanyl patches should ONLY be used to manage persistent, moderate to severe chronic pain that requires continuous, around-the-clock opiate administration for an extended period of time, and when the pain cannot be managed by other means such as non-steroidal analgesics, opiate combination products, or immediate-release opiates. Transdermal fentanyl should ONLY be used in patients who are already tolerant to opiate therapy, and who require a total daily dose of other opiates at least equivalent to a 25 mcg per hour fentanyl patch. Patients who are considered opiate-tolerant are those who have been taking, for a week or longer, at least 60 mg of morphine daily, at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily (or an equianalgesic dose of another opiate).

Initial dose
In selecting an initial dose, attention should be given to 1) the daily dose, potency, and characteristics of the opiate the patient has been taking previously, 2) the reliability of dose conversion guidelines featured in the package insert to

predict the potency of the fentanyl dose needed, 3) the degree of opiate tolerance, and 4) the patient's medical status. Equianalgesic dosing tables are available in the package insert for assistance. Overestimating the dose when converting patients from another opiate can result in a fatal overdose with the first dose.

Dose titration
During the initial patch application, patients should use short-acting analgesics as needed until efficacy with fentanyl is attained. There-after, some patients may still require short-acting analgesics for "breakthrough" pain. The starting doses listed in the equianalgesic tables are conservative to reduce the risk of overdosing patients on the first dose; 50% of patients may require a dose increase. The dose may be titrated upwards on the basis of the average daily use of a supplemental analgesic, but no more frequently than 3 days after the initial dose or every 6 days (after 2 patch applications) thereafter.

**The information provided is incomplete and should not be relied upon for prescribing. Full prescribing information can be found at: www.duragesic.com/duragesic/shared/pi/duragesic.pdf#zoom=100.

Videos Pertaining to Fentanyl Patches

- View the nNews report video provided by ISMP-Canada pertaining to fentanyl patchoverdoeses
- FDA video: Preventing Patient Deaths from Fentanyl Patches

200 Lakeside Drive, Suite 200, Horsham, PA 19044 , Phone: (215) 947-7797, Fax: (215) 914-1492