The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national nonprofit agency established for the collection and analysis of medication error reports and the development of recommendations for the enhancement of patient safety.

The Healthcare Insurance Reciprocal of Canada (HIROC) is a member-owned expert provider of professional and general liability coverage and risk management support.

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Transdermal Fentanyl: A Misunderstood Dosage Form

In 2004, two adolescent deaths were reported to be associated with the use of fentanyl patches (Duragesic) in Canada.[1] In the first case, fentanyl patches were prescribed for a 15-year-old girl for relief of chronic headache; the girl was found unresponsive 21 hours after the first patch was applied. In the second case, fentanyl patches were prescribed for a 14-year-old boy to treat severe sore throat due to mononucleosis; respiratory arrest occurred 14 hours after the first patch was applied. ISMP (US) has also received reports of deaths linked to the fentanyl patch in the United States.[2,3] In the fall of 2005, the manufacturer, Janssen-Ortho Inc., in consultation with Health Canada, issued advisories to health care professionals[4] and to the public[5] highlighting important information for the safe and appropriate prescribing and use of Duragesic. Examination of the ISMP Canada database of voluntarily reported medication incidents indicates ongoing problems with the use of fentanyl patches. As of July 27, 2006, there have been 122 reports classified as errors, and 12 of these (9%) resulted in patient harm.

Fentanyl is a highly potent opioid. **One transdermal fentanyl patch 25 mcg/hour provides comparable analgesia to a daily dose of 60 mg to 134 mg of oral morphine**.[6] Because of the risk of life-threatening hypoventilation, fentanyl patches are ***contraindicated*** for opioid-naïve patients. This drug should NOT be used in the management of acute or post-operative pain and is NOT recommended for children under 18 years of age. The fentanyl patch is ***indicated*** in the management of persistent, moderate to severe chronic pain that cannot be managed by other means such as oral opioid products and in patients who:

- need continuous (around-the-clock) opioid analgesia for an extended period of time, and
- are already receiving opioid therapy at a total daily dose equivalent to at least 60 mg oral morphine.

Fentanyl patches should not be used for patients who do not meet these criteria, nor should they be used where compliance with correct patch administration is in question or where follow-up monitoring for adverse effects is not possible. (The most up-to-date product monograph is available at http://www.janssen-ortho.com/JOI/en/product/products.asp.)

Types of Incidents Reported

Reports to ISMP Canada indicate that problems with the use of fentanyl patches exist in a variety of care settings (*e.g.*, hospitals, nursing homes, patient homes) and involve various stages in the medication use process: *prescribing* (*e.g.*, dose ordered not corresponding to manufacturer's available dose), *transcription* (*e.g.*, wrong patient, incorrect timeframe, omission of order to discontinue); *administration* (*e.g.*, previous patch not removed, dose omitted, incorrect administration times, incorrect dose), and *monitoring*. Although it is impossible to infer or project the probability of specific incidents on the basis of the voluntary reports received by ISMP Canada, the information available can be used to identify issues that may require additional investigation or attention.

Analysis of reports in the ISMP Canada medication incident database provides insight into the types of incidents reported as illustrated in Table 1.

Table 1. Transdermal fentanyl: types of incidents reported

Type of Incident	Total Number (%) Reported (*n*=122)	Number Reported with Harm
Incorrect dose	25 (20.5%)	4
Dose omission	54 (44.3%)	3
Incorrect duration	13 (10.7%)	2
Incorrect strength or concentration	5 (4.1%)	1
Incorrect time	14 (11.5%)	1
Other	11 (9%)	1

When combined with the qualitative information received, the following examples highlight areas of ongoing concern.

1) Patches not removed

> *"A patient was found to have new patches on their [sic] right upper arm, and old patches still on the left arm. The patient was responsive, but sluggish, with pinpoint pupils..."*
>
> *"Patient was found with a 25 microgram patch which had not been removed before an opioid infusion was started. The patient had two patches of 25 micrograms applied, and the nurse had removed only one before starting the infusion."*

Fentanyl patches are generally administered every 72 hours (every 3 days). The previous patch must be removed at the time of application of the new patch. Incidents reported include cases in which the patch was not removed at the time of the next dose, more than one patch was required for dosing but not all of the previous patches were removed at the time of administration of the next dose, cases in which the wrong transdermal patch (*i.e.*, wrong drug) was removed (from a patient receiving more than one drug by this mode of administration), and cases in which the patch was not removed when there was a change in the form of opioid therapy. After 72 hours, the fentanyl patch contains sufficient residual drug to potentially cause harm, particularly when combined with additional doses or other drugs with similar effects.

2) Patches manipulated for unusual doses

Dosing for elderly or debilitated patients may not be met by commercially available products. When very low dosages or unusual dose combinations are prescribed, practitioners may manipulate the patch to accommodate the prescribed dose. This may include cutting the patch, in the belief that this is the appropriate way to administer the correct dose. However cutting the patches can result in leakage and uncontrolled release of medication which could result in the absorption of a potentially fatal dose of fentanyl.[6] Commercially manufactured products with these low doses are not yet available in Canada, although at the time of writing Ortho-Janssen has received Health Canada approval to market Duragesic 12 mcg/h patch.

3) Patches not applied

"Patch not applied on due date and the omission was noted one day later. The patient experienced pain and required morphine."

Omission of doses may lead to a requirement for additional analgesia for pain control. Reports to the ISMP Canada database suggest that this can be problematic if the cause of the breakthrough pain is not recognized.

Contributing Factors

ISMP Canada, in conducting our analysis and receiving input from the reporters, has identified the following contributing factors:

- Lack of knowledge or awareness of indications and pharmacokinetics (effects of the fentanyl patch can continue for 24 hours or more following removal, due to the effect of a subcutaneous depot of fentanyl).
- Lack of understanding among practitioners, patients/residents, and families that this noninvasive route of fentanyl administration is highly potent.
- Use of doses requiring multiple patches of various strengths to be identified, calculated and administered.
- Use of fentanyl patches in combination with other opioid analgesics, CNS depressants (*e.g.*, benzodiazepines and sedating antihistamines), or drugs that affect the metabolism of fentanyl (*e.g.*,CYP 3A4 inhibitors increase or prolong the effect of fentanyl [e.g., erythromycin, diltiazem, clarithromycin, ketoconazole]).
- Application of a heat source to the patch (*e.g.*, heating pad, hot packs), resulting in increased release and absorption because of increased skin permeability. Fever may also enhance this potential.
- Lack of clear communication among multiple caregivers regarding
  - date, time, and location of application of a patch;
  - date and time when next patch is due to be applied.
- Inadvertent contact with the patch due to
  - lack of child-resistant packaging or failure to ensure secure storage alternatives;
  - patches falling off; and
  - unsafe disposal.[3,7]
- Prescription of smaller doses (or smaller dose increments) than are available from the manufacturer, which can lead to inappropriate manipulation of a patch, compromising its integrity and compromising the sustained release of fentanyl.

Recommendations

Recommendations to reduce medication incidents associated with fentanyl patches include the following:

- Apply the following criteria for the prescribing, dispensing, and administration of fentanyl patches[6]:
  - Use only for **adult** patients who are already receiving opioid therapy at a total dose of at least 60 mg/day oral morphine or its equivalent.
  - Use for the management of persistent, chronic moderate to severe pain, NOT for the management of acute or post-operative pain.
  - Use only for patients who require continuous (around-the-clock) opioid administration for an extended period of time.
  - Use only for patients whose pain cannot be managed by other means such as oral opioid products.
- Require a pharmacist to review all new orders for fentanyl patch before administration.
- Avoid having fentanyl patches available through override from automated dispensing cabinets.
- Ensure that the current documentation process clearly communicates the date, time, and location of patch administered and the date, time, and location of patch to be removed (*e.g.*, by providing prompts on the MAR).
- Provide an alert on the MAR for patients receiving more than one medication via the transdermal route.
- Assess pain management and check patch placement on each patient every shift.
- Ensure that policies, procedures, and guidelines on the use of transdermal fentanyl are readily available to practitioners and ensure that this documentation covers indications for use, requirements for monitoring, safe and secure disposal, and treatment and monitoring protocols in the event of toxic effects or overdose.
- Ensure that applicable alerts are generated from various sources (*e.g.*, automated dispensing cabinets, pharmacy computer systems, computerized physician order entry).
- Provide written information to the patient (*e.g.*, product monograph, part III: Consumer Information), and review instructions with patients and/or patient's family to ensure that important information is not overlooked and that they understand the risk of inappropriate handling of the product.

References:

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Canadian Anesthesiologists' Society Commitment to Sharing Information about Medication Incidents

The Canadian Anesthesiologists' Society (CAS) web homepage (www.cas.ca) now provides a link to the individual practitioner reporting component of the Canadian Medication Incident Reporting and Prevention System (CMIRPS), operated by the Institute for Safe Medication Practices Canada (www.ismp-canada.org/cmirps.htm).

Anesthesiologists are encouraged to report near misses or adverse medication incidents to the CMIRPS. Although each event may be unique, there are likely to be patterns in the sources of risk. The CAS Patient Safety Committee, working together with ISMP Canada, will use this information to identify needed system improvements and to establish practice recommendations, best practice guidelines and educational programs.

12-Month Fellowship on Safe Medication Management

ISMP Canada offers specialty fellowship learning and training in medication safety.

The fellowship curriculum includes:

- orientation to error reporting systems
- learning about principles and tools of interdisciplinary error prevention strategies
- contributing to publications and new projects
- activities in academia, research and education related to patient safety
- patient safety conference attendance
- working with ISMP Canada staff on medication safety projects
- opportunity to visit ISMP (US).

This fellowship offers an excellent stipend plus full benefits.

Qualifications: Applicants must be graduates of a health profession (e.g. pharmacy, nursing, medicine) with a keen interest in medication safety.

Qualified individuals are invited to send a completed application form and resume by September 30, 2006 to:

ISMP Canada
4711 Yonge Street, Suite 1600
Toronto, Ontario M2N 6K8
1-866-544-7672
Fax: 416-733-1146
email: info@ismp-canada.org

ISMP Canada is a national voluntary medication incident and 'near miss' reporting program founded for the purpose of sharing the learning experiences from medication errors. Implementation of preventative strategies and system safeguards to decrease the risk for error-induced injury and thereby promote medication safety in healthcare is our collaborative goal.

To report a medication error to ISMP Canada: (i) visit our website www.ismp-canada.org, or (ii) e-mail us at info@ismp-canada.org, or (iii) phone us at 416-480-4099. ISMP Canada guarantees confidentiality and security of information received. ISMP Canada respects the wishes of the reporter as to the level of detail to be included in our publications.

A Key Partner in the Canadian Medication Incident Reporting and Prevention System