



HEALTH CANADA ENDORSED IMPORTANT SAFETY INFORMATION
DURAGESIC* fentanyl transdermal system

September 13, 2005

SUBJECT: DURAGESIC* (fentanyl transdermal system) Safety Information

Dear Health Care Professional:

Janssen-Ortho Inc., in consultation with Health Canada, wishes to highlight certain important safety information for the safe and appropriate prescribing and use of DURAGESIC* (fentanyl transdermal system). There have been Canadian reports of deaths in people using DURAGESIC related to inappropriate use of the product outside of the conditions recommended in the Canadian Product Monograph, including reports of deaths related to the misuse and abuse of DURAGESIC. The Canadian Product Monograph for DURAGESIC has been revised to emphasize safety information. The Health Professional Information (Part I) and Consumer Information (Part III) sections of the new DURAGESIC Product Monograph are enclosed for your reference.

- ❖ Serious or life-threatening hypoventilation, including fatalities, has been reported in association with the use of DURAGESIC in Canada.
- ❖ Patients and their caregivers should be made aware of the signs and symptoms of fentanyl overdose and advised to seek medical attention immediately should signs and symptoms of fentanyl overdose be noted.
- ❖ DURAGESIC should not be used in patients who are opioid naïve, or in patients who require opioid analgesia for short-term, intermittent or post-operative pain.
- ❖ Use of DURAGESIC is not recommended in the pediatric population.
- ❖ Prescribers should be aware of the factors which may increase the potential for serious and life-threatening hypoventilation, and monitor and counsel patients and their caregivers appropriately. Such factors include fever, exposure to external heat sources, drug interactions, use of other CNS depressants including alcohol, and use in elderly and debilitated patients.
- ❖ The potential exists for misuse, abuse and diversion of DURAGESIC patches, and there have been Canadian reports of deaths involving misuse and abuse.
- ❖ Prescribers and pharmacists should communicate the importance of safe storage and proper disposal instructions to patients and their caregivers.

DURAGESIC Should Not be Used in Opioid-Naïve Patients

DURAGESIC is indicated for the management of persistent, moderate to severe chronic pain that cannot be managed by other means in patients who are already receiving opioid therapy at a total daily dose of at least 60 mg/day morphine equivalents. Conversion tables are provided to calculate the initial dose of DURAGESIC, which must not be higher than the equivalent total dose of opioids the patient is receiving at the time of switching to the patch.

Special Populations

Use of DURAGESIC is not recommended in the pediatric population. The use of DURAGESIC in children under 18 years of age is not recommended, as dosage requirements for the safe and efficacious use of DURAGESIC have not been established for this patient population. There have been Canadian reports of deaths in children using DURAGESIC.

Elderly and debilitated patients may have altered pharmacokinetics, which may require initiation of DURAGESIC therapy at a dose lower than that recommended by the conversion table.

Further recommendations for customization of therapy with DURAGESIC to specific clinical situations can be found in the Health Professional Information (Part I) section of the DURAGESIC Product Monograph.

Potential for Serious or Life-Threatening Hypoventilation

DURAGESIC contains a high concentration of a potent opioid, fentanyl, which along with other opioids of the morphine type has an associated risk of fatal overdose. The manifestations of fentanyl overdosage are an extension of its pharmacologic actions with the most serious effect being respiratory depression. Patients and their caregivers should be aware of the signs and symptoms of fentanyl overdose, and should be advised by prescribers and pharmacists to seek medical attention immediately should signs and symptoms of fentanyl overdose be noted.

Factors Increasing the Potential for Serious or Life-Threatening Hypoventilation

The potential for serious or life-threatening hypoventilation with DURAGESIC may be increased in patients who:

- use DURAGESIC concomitantly with potent cytochrome P450 3A4 inhibitors, such as ritonavir, ketoconazole, itraconazole, troleandomycin, clarithromycin, nelfinavir and nefazodone.
- use DURAGESIC in combination with CNS depressants (including other opioids, sedatives or hypnotics, general anesthetics, phenothiazines, tranquilizers), skeletal muscle relaxants, sedating antihistamines, and alcoholic beverages. Additive depressant effects may result.
- have fever; fentanyl concentrations could theoretically increase by approximately one-third for patients with a body temperature of 40°C (104°F) due to temperature-dependent increases in fentanyl release from the system and increased skin permeability.
- expose the DURAGESIC application site to direct external heat sources. All patients should be advised to avoid external heat sources such as heating pads, electric blankets, heated water beds, heat lamps, hot water bottles, saunas and hot whirlpool spa baths, intensive sunbathing, etc.
- use DURAGESIC other than in accordance with approved prescribing information.

Potential for Misuse, Abuse and Diversion

The potential exists for misuse, abuse and diversion of DURAGESIC patches. There have been Canadian reports of deaths involving misuse and abuse.

Alternative routes of administration and using damaged or cut DURAGESIC patches can potentially result in overdose from uncontrolled delivery of opioid. Prescribers should be aware that there have been reports of fentanyl abuse by ingestion, intravenous injection, volatilization and inhalation, or the application of multiple patches or use of patches prescribed for another individual. Prescribers should also be aware that a considerable amount of the drug remains in the patch after use and, therefore, the potential remains for misuse, abuse and diversion of used DURAGESIC patches.

Prescribers and pharmacists should communicate the importance of safe storage and proper disposal instructions to patients. Patients, family members and caregivers should be advised to protect DURAGESIC from theft or misuse in the work or home environment. The Canadian Product Monograph currently recommends folding the patch such that the adhesive side adheres to itself and flushing it down the toilet immediately after removing it from the skin. Any unused patches should be disposed of in the same manner.

Advice to Patients or Caregivers

The revised DURAGESIC Product Monograph contains an **Information for Patients** section which contains key safety instructions intended to be discussed by the prescriber with the patient, their family or caregiver, when prescribing DURAGESIC. Attention should be brought to the patient information sheet included in each package of DURAGESIC patches.

Health Professional Information (Part I) and Consumer Information (Part III) sections of the DURAGESIC Product Monograph are enclosed. The current Product Monograph is available on the Janssen-Ortho Inc. website at www.janssen-ortho.com and will be provided for the next edition of the *Compendium of Pharmaceuticals and Specialties*.

Adverse Event Reporting

Reporting rates determined on the basis of spontaneously reported post-marketing adverse events are generally presumed to underestimate the risks associated with drug treatments.

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse drug reaction reporting programmes. Any occurrences of serious and/or unexpected adverse reactions in patients receiving DURAGESIC should be reported to Janssen-Ortho Inc. or the Marketed Health Products Directorate at the following addresses:

Janssen-Ortho Inc.
19 Green Belt Drive
Toronto, Ontario M3C 1L9
Or call toll-free at 1-800-567-3331
Or email to dsscan@joica.jnj.com
Or toll-free fax to 1-866-767-5865

For other inquiries at Health Canada, please refer to contact information:

Marketed Health Products Directorate

MHPD_DPSC@hc-sc.gc.ca
Tel: (613) 954-6522 Fax: (613) 952-7738

Any suspected adverse incident can also be reported to:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario K1A 0K9
Local tel: 613-957-0337 or local fax: 613-957-0335
Toll-free tel: 1-866-234-2345 or toll-free fax: 1-866-678-6789
cadrmpp@hc-sc.gc.ca

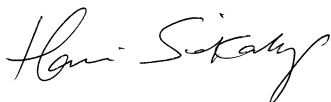
The ADR Reporting Form can be found in the Canadian *Compendium of Pharmaceuticals and Specialties* or on the TPD website along with the ADR Guidelines at:

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

Your professional commitment in this regard has an important role in protecting the well-being of your patients by contributing to early signal detection and informed drug use.

Should you have any questions or require additional information regarding the use of DURAGESIC, please contact Janssen-Ortho Inc. Medical Information Department at 1-800-567-3331 from 9:00 am to 5:00 pm Monday to Friday Eastern Standard Time (EST) or by facsimile at 416-449-2658. A copy of this letter is also available on the Janssen-Ortho website at www.janssen-ortho.com and on the Health Canada website at http://www.hc-sc.gc.ca/dhp-mps/medeff/index_e.html

Sincerely,



Hani Seikaly, Ph.D.
Director, Regulatory Affairs