Health Canada Endorsed Important Safety Information on Fentanyl Transdermal Systems

March 8, 2010

Dear Health Care Professional:

SUBJECT: New changes to the Dose Conversion Guidelines for Fentanyl Transdermal Systems

The manufacturers of Fentanyl Transdermal Systems (FTS) in collaboration with Health Canada wish to provide you with important new information regarding **changes to the Dose Conversion Guidelines (Table 1.1)** in the Dosage and Administration section of the Canadian Product Monographs for FTS.

- A 1:3 parenteral to oral morphine dose ratio replaces the previous 1:2 parenteral to oral morphine dose ratio, (e.g. 10 mg parenteral morphine = 30 mg oral morphine).
- The conversion doses of IV/IM morphine to Fentanyl Transdermal Systems for the 75, 87 and 100 mcg/hour patch strengths were revised to 'not applicable' to reflect the insufficiency of data available for guidance.
- The revised Dose Conversion Guidelines are provided below for your information and should be retained for future use. Changes have been highlighted for ease of reference.

Fentanyl, an opioid analgesic, is indicated for the management of persistent, moderate to severe chronic pain that cannot be managed by other means such as opioid combination products or immediate-release opioids. Fentanyl is to be used only in patients who require continuous around-the-clock opioid analgesia for an extended period of time and who are already receiving opioid therapy at a total daily dose of at least 60 mg/day oral Morphine Equivalents.

Changes to the Dose Conversion Guidelines reflect an update to the earlier changes outlined in the January 2009 Notice to Hospitals and Letter to Health Care Professionals [1, 2]. It should be noted that **all** Dose Conversion Guidelines are approximations, and knowledge of the overall clinical condition of the patient is critical for the selection of doses.

The Dose Conversion Guidelines are to be used to convert adult patients from their current oral or parenteral opioid analgesic only to the fentanyl transdermal patch. The Dose Conversion Guidelines are **unidirectional for use in chronic pain only**. They should **not be used to convert patients from FTS to other opioids**, as this may result in overdose and toxicity.

DOSAGE CONVERSION GUIDELINES FOR FENTANYL TRANSDERMAL SYSTEMS

Table 1.1 [1]: Dose Conversion Guidelines

To be used to convert from current opioid analgesic to the Fentanyl Transdermal Systems (FTS)

Current Analgesic	**Daily Dosage (mg/d)**						
Oral morphine	60-134	135-179	180-224	225-269	270-314	315-359	360-404
IM/IV morphine (based on a 1:3 IM/IV:PO ratio)	**20-44**	**45-60**	**61-75**	**76-90**	**NA[2]**	**NA[2]**	**NA[2]**
Oral oxycodone	30-66	67-90	91-112	113-134	135-157	158-179	180-202
Oral codeine	150-447	448-597	598-747	748-897	898-1047	1048-1197	1198-1347
Oral hydromorphone	8-16	17-22	23-28	29-33	34-39	40-45	46-51
IV hydromorphone[3]	4.0-8.4	8.5-11.4	11.5-14.4	14.5-16.5	16.6- 19.5	19.6-22.5	22.6-25.5
	⇓	⇓	⇓	⇓	⇓	⇓	⇓
Recommended Fentanyl Transdermal System (FTS) Dose	**25 mcg/h**	**37 mcg/h**	**50 mcg/h**	**62 mcg/h**	**75 mcg/h**	**87 mcg/h**	**100 mcg/h**

[1]Table 1.1 should not be used to convert from DURAGESIC and other FTS to other therapies because this conversion to DURAGESIC and other FTS is conservative. Use of Table 1.1 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, Safe Use of Tables 1.1, and 1.2).

[2] NA (not applicable) reflects insufficient data available for guidance**.** If needed, prescribers should make these conversions very carefully and conservatively.

[3] The conversion ratio of parenteral hydromorphone to oral hydromorphone of 1:2 is based on clinical experience in patients with chronic pain. Reference: Parenteral Drug Therapy Manual, Vancouver General Hospital, Pharmaceutical Sciences Clinical Services. 2006: Available from: http://www.vhpharmsci.com/PDTM/APDX11.htm.

Manufacturers of all fentanyl transdermal patches are working with Health Canada to include this safety information in the Dosage and Administration section in all Canadian Product Monographs for Fentanyl Transdermal Systems:

DURAGESIC® (fentanyl transdermal system)
TEVA-fentanyl
RAN-FENTANYL TRANSDERMAL SYSTEM
CO Fentanyl
Sandoz Fentanyl MTX Patch
DURAGESIC® MAT (fentanyl transdermal system)
ratio-FENTANYL Transdermal System
RAN-FENTANYL MATRIX PATCH
PMS-FENTANYL MTX

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any serious or unexpected adverse reactions in patients receiving fentanyl transdermal systems should be reported to the manufacturers or Health Canada at the following addresses:

Janssen-Ortho Inc.
Drug Safety Department
19 Green Belt Drive
Toronto, Ontario M3C 1L9
Telephone: (800) 567-3331
Fax: (866) 767-5865
dsscan@joica.jnj.com

Cobalt Pharmaceuticals Inc.
6500 Kitimat Road
Mississauga, Ontario L5N 2B8
Telephone: 1-866-254-6111
Fax: 905-542-0478

Teva Canada Limited
Pharmacovigilance and Drug Safety
30 Novopharm Court
Toronto, Ontario M1B 2K9
Telephone: 416-291-8888 ext. 5005
Fax: 416-335-4472
E-mail: PhV@tevacanada.com

Ranbaxy Pharmaceuticals Canada Inc.
2680 Matheson Blvd. East, Suite 200
Mississauga, Ontario L4W 0A5
Telephone: 1-866-840-1340
Fax: 905-602 4216

ratiopharm inc.
17800 Lapointe
Mirabel, Quebec J7J 1P3
Telephone: 1-800-337-2584
Fax: 1-800-313-7673
www.ratiopharm.ca
E-mail: drugsafety@ratiopharm.ca

Sandoz Canada Inc.
145, Jules Leger
Boucherville (Qc) J4B 7K8
Fax : 1-450-641-6408
E-mail: drugsafety.canada@sandoz.com

Pharmascience Inc.
Medical Information Dept.
6111 Royalmount Ave., Suite #100
Montreal, Quebec H4P 2T4
Telephone: 514-344-0764 or 1-888-550-6060
Fax: 1-514-340-0164
E-mail: adr@pharmascience.com

Any suspected adverse reaction can also be reported to:
Canada Vigilance Program
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
Ottawa, Ontario, K1A 0K9
Tel: 613-957-0337 or Fax: 613-957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866-234-2345
Fax: 866-678-6789
CanadaVigilance@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties.*

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei_form-eng.php

http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_fs-if/2009-ar-ei-guide-prof/index-eng.php

For other inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Tel: 613-954-6522
Fax: 613-952-7738

Please contact the appropriate manufacturer with any questions or concerns.

Authorized by:

Janssen-Ortho Inc.
Cobalt Pharmaceuticals Inc.
Teva Canada Limited
Ranbaxy Pharmaceuticals Canada Inc.
ratiopharm inc.
Sandoz Canada Inc.
Pharmascience Inc.

References:

[1] http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/fentanyl_nth-aah-eng.pdf
[2] http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/fentanyl_hpc-cps-eng.pdf