

Janssen-Ortho Inc.
Cobalt Pharmaceuticals Inc.
Novopharm Limited
Ranbaxy Pharmaceuticals Canada Inc.
ratiopharm inc.

**Health Canada Endorsed Important Safety Information on
Fentanyl Transdermal Systems**

January 2, 2009

Dear Health Care Professional:

SUBJECT: Important 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 information regarding changes to the **Dose Conversion Guidelines (Table 1.1)** and to the analgesic equivalency table: **Opioid Analgesics: Parenteral/Oral/Rectal Equianalgesic Potency Conversion (Table 1.2)** in the Dosage and Administration section of the Canadian Product Monographs for FTS. The **Dose Conversion Guidelines** are to be used to convert adult patients from their current oral or parenteral opioid therapy to the fentanyl transdermal patch. The analgesic equivalency table **Opioid Analgesics: Parenteral/Oral/Rectal Equianalgesic Potency Conversion**, may be used for adult patients taking opioids or doses not listed in Table 1.1, using the conversion methodology outlined for Table 1.1 with Table 1.2.

The revised **Dose Conversion Guidelines** and **Opioid Analgesics: Parenteral/Oral/Rectal Equianalgesic Potency Conversion Table** are attached for your reference and should be retained for future consultation. Changes have been highlighted for ease of reference.

Serious or life-threatening hypoventilation can result if appropriate conversions are not used.

Based on clinical experience in patients with chronic pain:

- The conversion from IM/IV morphine to the fentanyl transdermal patch has been revised to reflect a conversion ratio of 1:2 and 1:3 of parenteral morphine to oral morphine.
- The conversion from IV hydromorphone to the fentanyl transdermal patch has been revised to reflect a conversion ratio of 1:2 of parenteral hydromorphone to oral hydromorphone.

The use of fentanyl transdermal systems in opioid-naïve patients and in patients with acute or postoperative pain is contraindicated.

In addition, the analgesic equivalency table 1.2 has been revised to remove the data equating 10 mg parenteral morphine to 60 mg oral morphine derived from single or intermittent dosing studies. Data referring to IM/IV oxycodone and to IM meperidine have been removed from both Tables 1.1 and 1.2 as the former drug is not marketed in Canada as an injectable, and the latter drug causes CNS toxicity if used by the parenteral route chronically.

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)

CO Fentanyl

Novo-fentanyl

RAN-fentanyl transdermal system

ratio-FENTANYL Transdermal System

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 or 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

Novopharm 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@Novopharm.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

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/form/ar-ei_form_e.html

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

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.

Novopharm Limited

Ranbaxy Pharmaceuticals Canada Inc.

ratiopharm inc.

References

Johnson BL, Gross J. Chapter 8, Pharmacological Treatment of Cancer Pain in Handbook of Oncology Nursing, Jones & Bartlett Publishers, 1998. p.313-327

Ripamont, C, Pharmacology of Opioid Analgesia: Clinical Principles in Cancer Pain: Assessment and Management, edited by Bruera E and Portenoy RK. Cambridge University Press, 2003. p.124

Attachment

DOSAGE CONVERSION GUIDELINES FOR FENTANYL TRANSDERMAL SYSTEMS

Table 1.1^{1#}
From Current Opioid to DURAGESIC or other Fentanyl Transdermal Systems (FTS):
Dose Conversion Guidelines

Current Analgesic	Daily Dosage (mg/d)						
	Oral morphine	60-134	135-179	180-224	225-269	270-314	315-359
IM/IV morphine²	30-66	67-90	91-111	112-134	135-157	158-179	180-202
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 hydromorphone³	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

Alternatively, for adult patients taking opioids or doses not listed in Table 1.1, use the conversion methodology outlined above with Table 1.2.

[#] 12 mcg/h dose is not included in this table because it generally should not be used as the initiating dose, except in the case of patients for whom clinical judgment deems it appropriate to start DURAGESIC and other FTS at less than 25 mcg/h; DURAGESIC and other FTS at any dose is contraindicated in opioid-naïve patients (see **CONTRAINDICATIONS**).

¹Table 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, 1.2, and 1.3**).

² Based on clinical experience in patients with chronic pain, the conversion ratio of 10 mg parenteral morphine is equal to approximately 20 – 30 mg oral morphine. In the table above, calculation is based on a 1:2 parenteral to oral dose ratio. For some patients, a 1:3 parenteral to oral dose ratio (10 mg parenteral morphine = 30 mg oral morphine) may be more appropriate. The respective IM/IV morphine equivalents for the various fentanyl transdermal doses with a 1:3 ratio are:

IM/IV morphine (mg/d) at 1:3 parenteral to oral dose ratio	20-44	45-60	61-75	76-90	91-104	105 -119	120-134
Recommended FTS Dose	25 mcg/h	37 mcg/h	50 mcg/h	62 mcg/h	75 mcg/h	87 mcg/h	100 mcg/h

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.

**OPIOID ANALGESICS: PARENTERAL/ORAL/RECTAL
EQUIANALGESIC POTENCY CONVERSION**

Table 1.2
Opioid Analgesics: Parenteral/Oral/Rectal Equianalgesic Potency Conversion ⁽¹⁾

DRUG	Equivalent Dose (mg) ⁽²⁾ (compared to morphine 10 mg IM)		Duration of Action (hours)
	Parenteral	Oral	
Strong Opioid Agonists:			
Morphine (repeated dosing)	10	20-30 ⁽³⁾	3-4
Hydromorphone	1.5	7.5	2-4
Anileridine	25	75	2-3
Levorphanol	2	4	4-8
Oxymorphone	1	10 (rectal)	3-4
Methadone ⁽⁴⁾	---	---	---
Weak Opioid Agonists:			
Codeine	130	200	3-4
Oxycodone	---	30	2-4
Propoxyphene	50	100	2-4

⁽¹⁾ References:

Foley K.M. Cancer, Principles and Practice of Oncology, 4th Ed., V.T. Devita, Jr., S. Hellman, S.A. Rosenberg (Ed.), J.B. Lippincott Co., Philadelphia: 1993. p. 2417-2448.

Foley K. M. The Treatment of Cancer Pain, New Engl. J. Med. 313(2): 84-95, 1985.

Aronoff G.M Evans, W.O., Evaluation and Treatment of Chronic Pain, 2nd Ed., G.M. Aronoff (Ed.), Williams and Wilkins, Baltimore, p. 359-368, 1992.

Cherny N.I,Portenoy, R.K., Textbook of Pain, 3rd Ed., P.D. Wall and R. Melzack (Eds.), Churchill Livingstone, London, p. 1437-1467, 1994.

⁽²⁾ Most of these data were derived from single-dose, acute pain studies and should be considered an approximation for selection of doses when treating chronic pain.

⁽³⁾ The conversion ratio of 10 mg parenteral morphine = 20 – 30 mg oral morphine is based on clinical experience in patients with chronic pain.

Reference:

Skaer TL. Practice Guidelines for Transdermal Opioids in Malignant Pain. Drugs: 64 (23) 2629 – 2638, 2004.

Berdine HJ, Nesbit SA. Equianalgesic Dosing of Opioids. Journal of Pain & Palliative Care Pharmacotherapy: 20 (4) 79 – 84, 2006.

⁽⁴⁾ Extremely variable equianalgesic dose. Patients should undergo personalized titration starting at an equivalent to 1/10 of the morphine dose.