Drugs 2006; 66 (18): 2387-2393
0012-6667/06/0018-2387/$44.95/0

Fentanyl Buccal Tablet

In Breakthrough Pain in Opioid-Tolerant Patients with Cancer

Stephanie K.A. Blick and *Antona J. Wagstaff*

Wolters Kluwer Health | Adis, Auckland, New Zealand, an editorial office of Wolters Kluwer Health, Conshohocken, Pennsylvania, USA

Contents

Abstract

- The fentanyl buccal tablet (FBT) is a new formulation of fentanyl that uses an effervescent drug delivery system to enhance penetration across the buccal mucosa for the treatment of breakthrough pain in opioid-tolerant patients with cancer.
- Fentanyl is rapidly absorbed from FBT across the buccal mucosa and into the bloodstream.
- Fentanyl is more rapidly absorbed and bioavailability is higher from FBT than from the oral transmucosal fentanyl citrate formulation.
- In a well designed phase III trial in opioid-tolerant patients with cancer, a single dose of FBT 100–800μg provided clinically significant improvements in pain intensity from 15 to 60 minutes after the dose.
- Single FBT doses of 100–800μg were generally well tolerated; the majority of adverse events were mild to moderate in nature and typical of those associated with opioids.

Features and properties of fentanyl buccal tablet (FBT; Fentora™; CEP-25608)	
Indication	
Management of breakthrough pain in opioid-tolerant patients with cancer	
Mechanism of action	
μ-opioid–receptor agonist analgesic	
Dosage and administration	
Dose	100-800μg
Route	Buccal
Frequency	As needed for breakthrough pain; administration may be repeated once during a single breakthrough pain episode after 30 minutes if pain control is inadequate
Pharmacokinetic profile (single 800μg dose of FBT in healthy volunteers)	
Mean peak plasma concentration	1.6 ng/mL
Median time to peak plasma concentration	0.7h
Mean area under the plasma concentration-time curve from time zero to infinity	9.1 ng • h/mL
Median plasma elimination half-life	11.7h
Adverse events (incidence ≥5%)	
Most common	Nausea, dizziness, headache, fatigue, vomiting, somnolence, constipation and asthenia

Breakthrough pain is a discrete transitory episode of acute pain superimposed on a background of relatively well controlled, chronic pain.[1-3] Between 64% and 90% of patients referred to cancer pain centres with cancer-related pain experience breakthrough pain.[3] In the majority of cases, breakthrough pain is associated with cancer, and has been further categorised into three subtypes: incident, end-of-dose failure and idiopathic.[1,2] Incident breakthrough pain is induced by movement or a specific inciting activity, whereas end-of-dose failure breakthrough pain is associated with declining serum concentrations of around-the-clock analgesic medications; idiopathic breakthrough pain is unpredictable, having no obvious precipitant.[1-3]

Breakthrough pain is associated with impaired functioning and psychological distress, and its management needs to be preventative and active.[1-3] Relief from breakthrough pain can be derived from general measures, such as changing position, hot and cold compresses, massage, counselling and nonopioid analgesia; however, these practices provide modest relief at best.[2,3]

For most patients, the onset of breakthrough pain is rapid (measured in seconds to minutes), and orally administered supplemental analgesia takes too long to reach adequate concentrations.[1] Oral transmucosal fentanyl citrate, formulated as a solid drug matrix on a handle, has become a mainstay in the management of breakthrough pain because it provides faster absorption of fentanyl than achieved by regular oral formulations.[2] However, some limitations of this formulation include dental decay issues because of its sugar content, the fact that the time to reach a concentration for adequate pain relief is sometimes too long and limited compliance in debilitated patients.[2] It appears, therefore, that although oral transmucosal fentanyl citrate provides adequate management of breakthrough pain in opioid-tolerant patients with cancer, further refinement of this formulation would be a welcome addition to the medications currently available for this indication.

A novel delivery system (OraVescent® technology)[1] has been used to enhance transmucosal absorption of fentanyl across the buccal mucosa.[4] This delivery system produces a localised effervescent reaction that alters the pH in the buccal cavity to facilitate tablet solubilisation and, secondly, enhance permeation of un-ionised fentanyl across the buccal mucosa.[4]

This profile focuses on the pharmacological effects of the fentanyl buccal tablet (FBT; Fentora™) and the clinical efficacy of this medication for breakthrough pain in opioid-tolerant patients with cancer.

1. Pharmacodynamic Profile

The pharmacodynamic properties of fentanyl have been reviewed in detail elsewhere[5] and are thus only briefly summarised here.

- Fentanyl is a highly potent opioid agonist and acts primarily by interacting with μ-opioid-receptors;[5] it has no pharmacologically active metabolites.[6]
- The main pharmacological effects of fentanyl (analgesia and sedation) occur in the CNS, at μ-opioid-receptors throughout the brain and spinal cord; however, the precise mechanisms of opioid-induced analgesia are only partially understood.[5] Other secondary pharmacological CNS effects include anxiolysis, euphoria, miosis and cough suppression.[6]
- The analgesic potency of fentanyl is approximately 75–100 times greater than that of morphine, possibly because of the highly lipophilic nature of fentanyl, enabling it to transfer rapidly across the blood-brain barrier.[5] Fentanyl-induced analgesia and sedation appear to be dose-dependent.[5,6] Respiratory depression can occur with fentanyl at therapeutic doses, usually in non-opioid-tolerant patients.[5,6]
- Fentanyl may cause constipation through the binding of opioid agonists to opioid receptors in the gastrointestinal tract,[5] which causes a reduction in

1 The use of trade names is for product identification purposes only and does not imply endorsement.

stomach and duodenal motility, a decrease in propulsive peristaltic waves and an increase in tone.[6]

- Fentanyl may induce histamine release, with or without peripheral vasodilation and associated orthostatic hypotension, in some patients.[6]
- In animal studies, fentanyl was associated with additive or synergistic effects with clonidine,[7] α_2 adrenergic agonists,[8,9] pentobarbital[10] and diazepam;[11] naloxone blocks the effects of fentanyl.[12]

2. Pharmacokinetic Profile

The absorption and bioavailability of fentanyl from FBT have been evaluated in five clinical trials. Two of these trials compared the pharmacokinetic properties of FBT with those of oral transmucosal fentanyl citrate.[13,14] The trials were prospective, randomised, nonblind trials in healthy, non-opioid-tolerant volunteers (n = 25–39) who received single 100–1300μg doses of FBT.[4,13-16] A retrospective analysis of data from two of these trials[4,13] is also included in this review.[17] Naltrexone was administered to participants in all trials to block the opioid receptor–mediated effects of fentanyl. Venous samples were taken before fentanyl administration and over 36–72 hours afterward; fentanyl was analysed using high-performance liquid chromatography with tandem mass spectroscopy. Currently, one analysis is available as an abstract with poster.[17]

The distribution, metabolism and excretion of fentanyl are well known[5] and described only briefly here.

- FBT uses a novel delivery system, OraVescent® technology, to produce an effervescent reaction that liberates carbon dioxide in the buccal cavity.[4,18] This reaction causes an initial decrease in pH, which facilitates solubilisation, thus driving fentanyl into solution.[4,19] The subsequent release of carbon dioxide increases the local pH, which optimises permeation of un-ionised fentanyl across the buccal mucosa.[4,13,18,19]
- Fentanyl is rapidly and extensively absorbed from FBT across the buccal mucosa and into the bloodstream.[4,13-16] After administration of a dose of 400μg to healthy volunteers, mean maximum plasma concentrations (C_{max}; 0.94–1.03 ng/mL[14-16]) were reached in 0.58–0.78 hours (median time to maximum concentration [t_{max}]).[14-16] With doses of 100–810μg, C_{max} values increased dose-proportionally,[4,13,16] whereas increases were less than dose-proportional with higher doses.[4,13] Following a single FBT dose of 800μg in healthy volunteers, mean C_{max} was 1.6 ng/mL and median t_{max} was 0.7 hours.[16] Across the five trials, median t_{max} values ranged from 0.58 to 1.5 hours, irrespective of dose.[4,13-16]
- The area under the plasma concentration-time curve from time zero to infinity (AUC_∞) increased dose-proportionally with all doses.[4,13,16] For an FBT dose of 400μg, the AUC from time zero to the median t_{max} ($AUC_{tmax'}$) of a reference dose of 100 or 400μg was 0.34–0.36 ng • h/mL.[15,16] Following an 800μg dose, the mean AUC_∞ was 9.1 ng • h/mL.[16] In addition, an increase in the fentanyl AUC is expected with coadministration of ritonavir in humans, although coadministration of ritonavir with buccal fentanyl has not been studied.[6]
- Systemic exposure to fentanyl after a single dose of FBT 1080μg was significantly ($p < 0.001$) greater than that achieved after a single dose of oral transmucosal fentanyl citrate 1600μg (figure 1).[13] In comparisons of FBT 400μg with oral transmucosal fentanyl citrate 800μg, the dose-normalised (i.e. to a 400μg fentanyl dose) mean values for C_{max} (1.02 ng/mL) and $AUC_{tmax'}$ (0.4 ng • h/mL) for FBT were numerically higher than those for oral transmucosal fentanyl at 800μg (0.63 ng/mL and 0.14 ng • h/mL).[14] In addition, the median t_{max} for FBT was approximately half that of oral transmucosal fentanyl citrate and oral fentanyl.[14]
- In healthy volunteers, the absolute bioavailability of fentanyl from a single dose of FBT (400μg) was greater than that from oral transmucosal fentanyl citrate (800μg) or oral fentanyl (800μg) based on the ratios of the respective AUC_∞ values to the AUC_∞ value of 400μg of intravenous fentanyl (0.65 vs 0.47 and 0.31).[14] Furthermore, FBT was absorbed in approximately equal proportions through the buccal mucosa (48%) and the gastrointestinal tract (52%), whereas with oral transmucosal fentanyl citrate, the

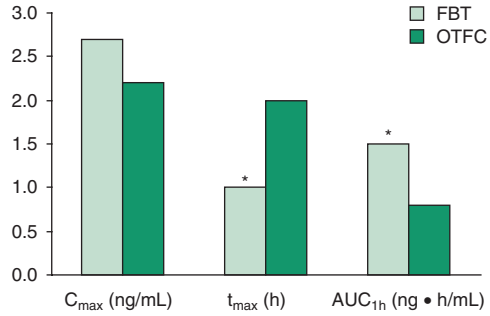

Fig. 1. Absorption pharmacokinetic parameters of fentanyl buccal tablet (FBT) relative to those of oral transmucosal fentanyl citrate (OTFC). Results from a randomised, nonblind, single-dose study in healthy volunteers (n = 40) who received FBT 1080μg or OTFC 1600μg.[13] AUC_{1h} was chosen because the median t_{max} for the reference dose of buccal fentanyl 810μg was 1h. **AUC_{1h}** = area under the serum concentration-time curve from time zero to 1h; **C_{max}** = mean maximum serum fentanyl concentration; **t_{max}** = median time to C_{max}. * $p < 0.001$ vs OTFC.

proportion absorbed through the buccal mucosa (22%) was lower than that absorbed gastrointestinally (78%).[14]

- A crossover bioequivalence study[15] found that C_{max} and AUC_{∞} values, but not t_{max}, were slightly higher with four FBT 100μg tablets than with one 400μg tablet, possibly because of the relative increase in the overall surface area after administration of multiple tablets simultaneously.

- Fentanyl is 79–87% protein bound in plasma (human data) and is widely and rapidly distributed into the brain, heart and lungs (animal data).[5] Following gastrointestinal absorption and an elimination phase, a final, slower phase of redistribution between serum and both muscle and adipose tissue takes place.[4] After administration of FBT ≤500μg, a biexponential decrease in fentanyl plasma concentrations from mean C_{max} was observed, whereas after doses of ≥800μg, this decrease was triexponential.[4,16]

- The terminal elimination half-life ($t_{1/2}$) of FBT varied widely with dose, particularly at lower doses. Over a single-dose range of 100–800μg, the median $t_{1/2}$ of fentanyl ranged from 3 to 14 hours.[15,16] Similarly, over a dose range of 200–1300μg, the mean $t_{1/2}$ was 6.5–13 hours.[4,13] The $t_{1/2}$ appeared to reach a relative plateau at higher doses ($t_{1/2}$ was 3–7 hours for 100–270μg doses and 11–14 hours for 400–1300μg doses).[4,13,15,16] This wide range is thought to reflect differences in elimination of fentanyl from muscle and adipose tissue.[4]

- Wide interindividual variations in the $t_{1/2}$ of FBT were also noted ($t_{1/2}$ ranged from 1–5 hours for some volunteers receiving single doses of 100–800μg to 14–32 hours in others over the same dose range); the median plasma elimination half-life following a single 800μg dose was 11.7 hours.[15,16]

- Dwell time, the time between placement of the tablet and its complete disappearance from the oral cavity, does not appear to affect the pharmacokinetics of FBT.[17] The rate and extent of the buccal absorption of FBT were not correlated with dwell time, which showed high interindividual variability (mean 14–25 minutes, range 3–62 minutes).[17]

3. Therapeutic Efficacy

The therapeutic efficacy of FBT in cancer-related breakthrough pain has been investigated in one fully published, randomised, double-blind, placebo-controlled, multicentre trial.[20] Preliminary efficacy results from clinical trials of FBT in patients with breakthrough pain not associated with cancer have also been reported; however, since FBT is indicated specifically for cancer-related breakthrough pain, these trials will not be discussed further here.[21-25]

Inclusion criteria included a diagnosis of a haematological malignancy or malignant solid tumour, opioid tolerance and one to four episodes of cancer-related breakthrough pain per day.[20] Opioid tolerance was defined as receiving oral morphine 60–1000 mg/day, or an alternative oral opioid of equivalent dosage or transdermal fentanyl 50–300 μg/day, for ≥1 week.[20] Exclusion criteria included intrathecal opioid treatment, grade 2 or greater mucositis or stomatitis or a lack of association of the primary source of breakthrough pain with cancer.[20]

In the initial open-label dose-finding period, FBT was titrated to a dose that effectively managed two consecutive episodes of breakthrough pain.[20] The doses available were 100, 200, 400, 600 and 800μg. The highest tolerated dose was ineffective in 20 of 123 enrolled patients in this phase.[20] Eligible pa-

tients (n = 77) then received 1 of 18 predefined dose sequences of ten tablets (seven FBT and three placebo), using the predetermined effective dose, to manage up to four episodes of breakthrough pain per day, within a 21-day period.

Pain intensity (PI) was measured on an 11-point scale (0 = no pain, 10 = worst pain).[20] The differences in PI after and before drug administration (PID) were summed (SPID), and the primary efficacy variable was SPID at 30 minutes. Other analyses included patient's global performance rating of the medication (GMP) at 30 and 60 minutes using a 5-point scale (0 = poor, 4 = excellent), SPID at 15, 45 and 60 minutes, pain relief (5-point scale; 0 = none, 4 = complete) and summed total pain relief.[20]

- SPID was significantly higher with FBT than with placebo at 30 minutes (3.0 vs 1.8; $p < 0.0001$) and at all other recorded timepoints ($p < 0.01$ at 15 minutes, $p \leq 0.0001$ at 45 and 60 minutes).[20] In the evaluable population (n = 72), a total of 701 episodes of breakthrough pain were observed (493 treated with FBT and 208 for which placebo was taken).[20]

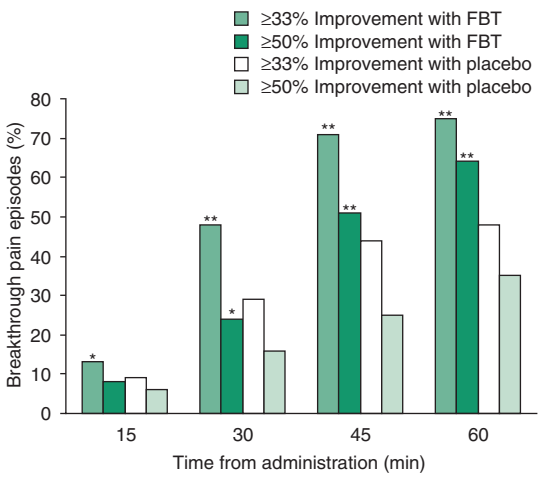

Fig. 2. Therapeutic efficacy of fentanyl buccal tablet (FBT). Percentage of breakthrough pain episodes showing an improvment (≥33% or ≥50% reductions) from baseline in pain intensity scores, measured on an 11-point scale at various time points for each pain episode. For breakthrough pain episodes in patients with cancer (n = 72), FBT (n = 493 episodes) or placebo (n = 208 episodes) was administered in a double-blind, multicentre trial.[20] * $p < 0.05$, ** $p < 0.0001$ vs placebo.

- Significant differences favouring FBT over placebo were also observed in the mean scores for PID, pain relief, and total pain relief at all timepoints ($p < 0.01$ at 15 minutes; $p \leq 0.0001$ at 30, 45 and 60 minutes).[20]
- Moreover, clinically significant improvements in PI scores (i.e. reductions of ≥33% and ≥50%) were observed in a greater proportion of FBT-treated breakthrough pain episodes than episodes for which placebo was taken ($p < 0.05$ for all timepoints except for ≥50% at 15 minutes; figure 2).[20]
- GMP ratings were significantly higher with FBT than with placebo at 30 and 60 minutes ($p < 0.0001$ for both).[20] Furthermore, the patient ratings showed greater satisfaction with FBT from 30 to 60 minutes, suggesting a continued improvement over time.[20]
- Supplemental medication was more than twice as likely to be required with placebo than with FBT (50% vs 23% of episodes; relative risk ratio 0.47; 95% CI 0.37, 0.60).[20]
- Titration appears more effective than the use of a percentage of an around-the-clock opioid dose for establishing the dose of FBT.[20] No meaningful correlation was observed between the effective dose of FBT and the equivalent analgesic opioid dosage or previous supplemental opioid dose.[20]

4. Tolerability

The safety and tolerability of FBT were examined in 123 patients in a randomised, double-blind, placebo-controlled, multicentre trial (see section 3).[20] In addition, tolerability data were obtained from an interim analysis of a tolerability study available as an abstract with poster.[26] In the latter study, 170 of 207 recipients of FBT 100–800μg received long-term (mean ≈3.5 months) treatment.[26]

- In general, FBT 100–800μg was well tolerated; most adverse events were of a mild-to-moderate nature and typical of adverse effects associated with opioids.[20,26]
- In the phase III trial, the most commonly reported adverse events (reported in ≥5% of the study population; n = 123) were nausea (22%), dizziness (22%), headache (15%), fatigue (12%), vomiting

(11%), somnolence (10%), constipation (8%) and asthenia (7%).[20]

- Of 170 evaluable patients with long-term (mean ≈3.5 months) data who received a mean 539μg dose per episode of breakthrough pain, 32% reported a treatment-related adverse event, none of which was serious.[26]
- Oral mucosal ulcers at the application site led to study withdrawal in 2 of 123 patients in the phase III trial[20] and in 4 of 207 patients in the long-term tolerability study.[26]

5. Dosage and Administration

FBT is indicated for the management of breakthrough pain in patients with cancer who are already receiving and are tolerant of opioid therapy for their underlying persistent cancer pain.[6] Opioid tolerance is defined as the consumption of ≥60mg oral morphine per day, or an equivalent analgesic dose of another opioid, for at least a week.

FBT is available as tablets in strengths of 100, 200, 400, 600 and 800μg. It is recommended that administration be tailored to the patient's individual requirements through dose titration to provide effective analgesia with tolerable adverse effects.[6] Titration should start with multiples of the 100μg tablet.[6] During a single episode of breakthrough pain, if pain is not adequately relieved, dosing may be repeated once after 30 minutes.[6] Dose adjustment may be necessary if switching from oral transmucosal fentanyl citrate to FBT because of higher bioavailability (see section 2).

The manufacturer's prescribing information for FBT, a Schedule II controlled substance, contains a black-box warning about the abuse liability of opioid analgesics.[6] The warning also cautions that, because life-threatening respiratory depression can occur with any opioid dosage in patients who are not opioid tolerant, FBT is contraindicated for management of acute or postoperative pain and is not indicated for use in non-opioid-tolerant patients.[6]

For further comprehensive dosage and administration guidelines and contraindications, the local manufacturer's prescribing information should be consulted.

6. Fentanyl Buccal Tablet: Current Status in Breakthrough Pain Associated with Cancer

FBT has been approved by the US FDA for the treatment of breakthrough pain in opioid-tolerant patients with cancer. In a well designed trial, FBT (100–800μg) was effective in controlling breakthrough pain and was generally well tolerated.

Disclosure

During the peer review process, the manufacturer of the agent under review was also offered an opportunity to comment on this article; changes based on any comments received were made on the basis of scientific and editorial merit.

References

1. Portenoy RK, Payne D, Jacobsen P. Breakthrough pain: characteristics and impact in patients with cancer pain. Pain 1999 May; 81: 129-34
2. Fine PG. Breakthrough cancer pain: epidemiology, characteristics and management. CNS Drugs 2000 May; 13: 313-9
3. Mercadante S, Arcuri E. Breakthrough pain in cancer patients: pathophysiology and treatment. Cancer Treat Rev 1998 Dec; 24: 425-32
4. Darwish M, Tempero K, Kirby M, et al. Pharmacokinetics and dose proportionality of fentanyl effervescent buccal tablets in healthy volunteers. Clin Pharmacokinet 2005; 44 (12): 1279-86
5. Muijsers RBR, Wagstaff AJ. Transdermal fentanyl: an updated review of its pharmacological properties and therapeutic efficacy in chronic cancer pain control. Drugs 2001; 61 (15): 2289-307
6. Cephalon Inc. Prescribing information for Fentora™ (fentanyl buccal tablet). Available from URL: http://www.fda.gov/cder/foi/label/2006/021947lbl.pdf [Accessed 2006 Sep 23]
7. Horváth G, Benedek G, Szikszay M. Enhancement of fentanyl analgesia by clonidine plus verapamil in rats. Anesth Analg 1990; 70: 284-8
8. Horváth G, Szikszay M, Rubicsek G, et al. An isobolographic analysis of the hypnotic effects of combinations of dexmedetomidine with fentanyl or diazepam in rats. Life Sci 1992; 50: PL215-20
9. Hu C, Flecknell PA, Liles JH. Fentanyl and medetomidine anaethesia in the rat and its reversal using atipamazole and either nalbuphine or butorphanol. Lab Animals 1992; 26: 15-22
10. Yaster M, Keohler RC, Traystman RJ. Interaction of fentanyl and pentobarbital on peripheral and cerebral hemodynamics in newborn lambs. Anesthsiology 1989; 70: 461-9
11. Reves JG, Kissin I, Fournier SE, et al. Additive negative ionotropic effect of a combination of diazepam and fentanyl. Anesth Anal 1984; 63: 97-100
12. Brown JH, Pleuvry BJ. Antagonism of the respiratory effects of alfentanil and fentanyl by naloxone in the conscious rabbit. Br J Anaesth 1981; 53: 1033-7

13. Darwish M, Tempero K, Kirby M, et al. Relative bioavailability of the fentanyl effervescent buccal tablet (FEBT) 1080 micrograms versus oral transmucosal fentanyl citrate 1600 micrograms and dose proportionality of FEBT 270 to 1300 micrograms: a single-dose, randomized, open-label, three-period study in healthy adult volunteers. Clin Ther 2006 May; 28 (5): 715-24

14. Darwish M, Kirby M, Robertson P, et al. Absolute and relative bioavailability of fentanyl buccal tablet and oral transmucosal fentanyl citrate. J Clin Pharmacol. In press

15. Darwish M, Kirby M, Robertson Jr P, et al. Comparison of equivalent doses of fentanyl buccal tablets and arteriovenous differences in fentanyl pharmacokinetics. Clin Pharmacokinet 2006; 45 (8): 843-50

16. Darwish M, Kirby M, Robertson Jr P, et al. Pharmacokinetic properties of fentanyl effervescent buccal tablets: a phase I, open-label, crossover study of single-dose 100, 200, 400, and 800 micrograms in healthy adult volunteers. Clin Ther 2006 May; 28 (5): 707-14

17. Darwish M, Kirby M, Jiang JG. Effect of dwell time on the pharmacokinetics of fentanyl effervescent buccal tablets [abstract no. P-37E plus poster]. American Society of Health-System Pharmacists' Summer Meeting; 2006 June 25-28; Orlando (FL)

18. Eichman JD, Robinson JR. Mechanistic studies on effervescent-induced permeability enhancement. Pharm Res 1998; 15 (6): 925-30

19. Durfee S, Messina J, Khankari R. Fentanyl effervescent buccal tablets: enhanced buccal absorption. Am J Drug Deliv 2006; 4 (1): 1-5

20. Portenoy RK, Taylor D, Messina J, et al. A randomized, placebo-controlled study of fentanyl buccal tablet for breakthrough pain in opioid-treated patients with cancer. Clin J Pain 2006 Nov/Dec; 22 (9): 805-11

21. Webster L, Taylor D, Peppin J, et al. Open-label study of fentanyl effervescent buccal tablets in patients with noncancer pain and breakthrough pain: patient preference assessment [abstract no. 804 plus poster]. J Pain 2006 Apr; 7 4 Suppl. 2. Plus poster presented at the American Pain Society's annual meeting; 2006 May 3-6; San Antonio, (TX): S52

22. Hale M, Webster L, Peppin J, et al. Open-label study of fentanyl effervescent buccal tablets in patients with chronic pain and breakthrough pain: interim safety and tolerability results [abstract no. 3040 plus poster]. American Academy of Pain Medicine's Annual Meeting; 2006 Feb 22-25; San Diego (CA)

23. Nalamachu S, Messina J, Xie F. Evaluation of patients' preference for fentanyl effervescent buccal tablets to manage breakthrough pain [bstract no. 06-A-1883-AAPMR]. American Academy of Physical Medicine and Rehabilitation; 2006 Nov 9-12; Honolulu (HI)

24. Nalamachu S, Messina J, Xie F. Impact of fentanyl effervescent buccal tablets on mood, functioning, and quality-of-life in patients with breakthrough pain [abstract no. 06-A-1874-AAPMR]. American Academy of Physical Medicine and Rehabilitation; 2006 Nov 9-12; Honolulu (HI)

25. Portenoy RK, Xie F, Messina J, et al. Fentanyl buccal tablet (FBT) for the treatment of breakthrough pain in opioid-treated patients with chronic low back pain: a randomized, placebo-controlled study [abstract plus poster]. American Society of Regional Anesthesia and Pain Medicine; 2006 Nov 16-19; San Francisco (CA)

26. Slatkin N, Charu V, Niebler G, et al. Long-term tolerability of fentanyl effervescent buccal tablets: interim analysis in patients with cancer-related breakthrough pain. [abstract no. 8567 plus poster] American Society of Clinical Oncology's 42nd Annual Meeting; 2006 June 2-6; Atlanta (GA): 484

Correspondence: *Stephanie K.A. Blick*, Wolters Kluwer Health | Adis, 41 Centorian Drive, Private Bag 65901, Mairangi Bay, Auckland 1311, New Zealand.
E-mail: demail@adis.co.nz