Translated from *Rev Prescrire* September 2011; 31 (335): 651

fentanyl nasal

NEW DRUG

Still no tangible advantage of intranasal administration

● **No better than immediate-release oral *morphine* in a trial including 84 patients, but more frequent adverse effects. Risk of overdose due to confusion between the different forms and doses of *fentanyl*.**

NOTHING NEW

Immediate-release oral *morphine* is the standard option for cancer patients with breakthrough pain despite appropriate opioid therapy (1). Alternatives include three forms of buccal *fentanyl* (1). There is no evidence that intranasal *fentanyl* (Instanyl°) is more effective or better tolerated than buccal *fentanyl*. Mid 2011, the packaging posed a risk for both patients and caregivers (1).

A second form of *fentanyl* nasal spray (Pecfent°, Archimedes) has been announced. The solution contains pectin and sucrose and is designed to form a gel coating on the nasal mucosa after application (2). The following article examines whether this second intranasal *fentanyl* product provides more rapid or more effective relief than immediate-release oral *morphine* or buccal *fentanyl* for cancer patients with breakthrough pain, and whether the packaging of Pecfent° is better designed than that of Instanyl°.

A trial versus immediate-release oral morphine. In addition to a placebo-controlled trial (although ethically unacceptable in this setting), the new form of intranasal *fentanyl* has been evaluated in a small trial (84 patients) versus immediate-release oral *morphine* (**a**)(2,3). In the 79 patients who completed the trial, the mean difference in pain intensity, assessed 15 minutes post-dose on a 10-point rating scale (primary endpoint), was 3.0 points in the intranasal *fentanyl* group versus 2.7 points in the *morphine* group (3). Although statistically significant, this slight difference is not clinically relevant.

Adverse effects (mainly vomiting, drowsiness, dehydration and nausea) occurred in about half of the patients treated with intranasal *fentanyl*, versus 16% of those treated with *morphine* (3). Three patients treated with intranasal *fentanyl* experienced serious adverse effects (hypotension, heart failure, and anuria), versus none in the *morphine* group (3).

About one-quarter of the 523 patients treated with intranasal *fentanyl* in clinical trials experienced opioid-related adverse effects or effects associated with nasal administration (epistaxis, runny nose, or nasal discomfort) (2).

Better-designed packaging but an incomplete dose range. Pecfent° is sold in multidose spray bottles equipped with a metered-dose pump that has to be primed for initial use, as with Instanyl°. The pump has a spray counter so that the patient can hear a click and see that the pump has been primed, and track the number of doses administered. This is an advantage, but a system ensuring a lock-out period between two doses would also be useful.

The lack of a 300-µg dose strength rules out the use of doses of 300 or 600 µg.

In clinical trials, 8% to 16% of patients had difficulty using the device (2).

Only the box, and not the bottle, is child-resistant.

Used bottles are to be returned to a pharmacy for disposal (4). They must not be placed in the household waste because they still contain enough *fentanyl* to cause harm.

The increased number of *fentanyl* products and dose strengths represents a source of confusion and overdose, especially as the different formulations are not bioequivalent (1,4).

fentanyl

PECFENT°

Nasal spray solution

• **100 µg** or **400 µg** of *fentanyl* per spray

opioid analgesic

■ **Indication:** *"breakthrough pain (BTP) in adults who are already receiving maintenance opioid therapy for chronic cancer pain".*
[EU marketing authorisation, centralised procedure]

In practice. It is better to prescribe immediate-release oral *morphine*, or possibly buccal *fentanyl,* to cancer patients with breakthrough pain.

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a- After a titration phase with intranasal fentanyl, the patients were randomised to receive, in double-blind manner, the following treatments to treat 10 pain exacerbations: 5 bottles of intranasal fentanyl to take each time with 1 placebo capsule, and 5 bottles of intranasal placebo to take each time with 1 capsule of immediate-release morphine (refs 2,3).

Selected references from Prescrire's literature search.

In response to our request for information, Archimedes provided us only with published documents and packaging items.

1- Prescrire Editorial Staff "Intranasal fentanyl. Breakthrough cancer pain: unsafe packaging" *Prescrire Int* 2010; **19** (110): 251.
2- European Medicines Agency – CHMP "Assessment report for Pecfent. EMEA/H/C/1164": 62 pages; posted on the EMA website 14 September 2010.
3- HAS – Commission de la transparence "Avis-Pecfent" 16 February 2010: 12 pages.
4- European Commission "Commission decision – Pecfent. Summary of product characteristics + package leaflet": 59 pages.

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