

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 signifi-

cant, 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- μ g dose strength rules out the use of doses of 300 or 600 μ g.

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 μ g or 400 μ g 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.