

DRUG UPDATE

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FENTANYL PATCHES

Fentanyl is a potent opioid analgesic which can be administered transdermally. In comparative trials, fentanyl patches had similar efficacy and adverse effects to sustained-release morphine tablets however, there is limited evidence to suggest that fentanyl is associated with less constipation. Sustained-release oral morphine is the opioid of first choice for moderate to severe chronic pain. Fentanyl patches should be reserved for patients with stable opioid requirements who are unable to tolerate oral medications.

What is it?

Fentanyl patches (Durogesic®, Janssen Cilag) are licensed for the management of chronic intractable cancer and non-cancer pain.¹ The patches are available in four different strengths and are designed to deliver the drug at a constant rate of 25, 50, 75 or 100 mcg/hr. Each patch requires replacement every 3 days.¹ A 25 mcg fentanyl patch is approximately equivalent to 90 mg/day of morphine sulphate.²

How effective is it?

The efficacy of fentanyl patches for chronic cancer pain has been evaluated in one placebo-controlled study and 2 comparative studies with sustained release morphine.³⁻⁵

In the placebo-controlled study, a total of 138 patients initially received transdermal fentanyl at doses titrated over 15 days to achieve adequate pain control with acceptable tolerability.³ Patients with no worse than moderate pain were then randomised to receive double-blind treatment with either placebo patches (n=48) or fentanyl patches (n=47) at a fixed dose (median dose of 50 mcg) for 9 days. Patients were allowed to take non-opioid analgesics and rescue oral morphine. Nine patients (19%) treated with fentanyl and 13 patients (27%) on placebo were withdrawn because of inadequate pain control (p=0.254). No significant difference was observed in the number of patients experiencing effective pain control between the fentanyl or placebo groups (66% vs 48%, p=0.071).³

The first comparative study was an open-label, crossover study in which 202 patients were randomised to receive either transdermal fentanyl or sustained-release oral morphine for 15 days followed immediately by the other analgesic for a further 15 days.⁴ The main objective of the study was to assess patients' preference for the two treatments. Pain control was evaluated using 2 validated scoring systems and patients' diary recordings. A total of 110 patients completed the study, of which 50 had received fentanyl in the first phase and 60 in the second phase of treatment. There were no significant differences in pain control between the fentanyl and morphine phases with 77% of patients on fentanyl and 81% on morphine recording adequate pain control. Patients required rescue analgesia more often with fentanyl than with morphine, on an average of 8 out of 15 days (53.9%) versus 6 out of 15 days (41.5%) (p=0.0005). In addition, more patients needed an upward titration of their fentanyl dose suggesting that the

doses used were insufficient.⁴ Of those patients who were able to express a view (n=136), 14 (10%) had no preference, 73 (54%) preferred fentanyl, and 49 (36%) preferred morphine (p=0.037), however bias cannot be excluded as this was an open-label study.⁴

In the second study, 47 terminal cancer patients received oral morphine immediate-release for 7 days, prior to randomisation to open-label morphine sustained-release or fentanyl patches for a further 14 days with doses titrated according to response.⁵ A verbal four-point ranking scale was used to monitor pain control. Forty patients completed the study, 20 in each group. There was no significant difference in either analgesic efficacy or use of rescue analgesia between the two groups.⁵

Long-term data comparing fentanyl patches with other analgesics are not available. The long-term efficacy of morphine is well established in chronic cancer pain. Current data on the long-term efficacy of fentanyl in chronic cancer pain is limited to uncontrolled studies.^{6,7}

How safe is it?

Fentanyl patches were associated with similar adverse effects to oral morphine in the largest open-label comparative study.⁴ Common events reported during treatment were nausea (32 with fentanyl versus 23 with morphine), vomiting (18 with both fentanyl and morphine) and drowsiness (17 versus 19). There was no significant difference between the two treatment groups. However, fentanyl was associated with a lower incidence of constipation. During the fentanyl treatment phase, 45 (27.2%) patients reported constipation versus 69 (44.5%) patients during treatment with morphine (p=<0.001).⁴ Studies have suggested that patients who are switched from oral morphine to transdermal fentanyl require fewer laxatives.^{8,9}

Following long-term use with transdermal fentanyl, four cases of mild respiratory depression were recorded and there are case reports of severe respiratory depression and sedation.^{7,10} A recent report describes four case studies in which advanced cancer patients on transdermal fentanyl developed delayed and severe respiratory depression and sedation.¹¹

Elderly, cachectic, or debilitated patients should be observed for signs of fentanyl toxicity and the dose reduced if necessary.¹

Used patches may contain enough residual fentanyl (24-84% of the starting dose depending on individual patient) to cause serious toxicity in children, opioid-naïve patients and pets.¹² This emphasises the need for adequate patch disposal via incineration, flushing down the toilet or cutting them up. Patients should be educated in these disposal methods.¹³

What other options are there?

Sustained-release oral morphine is the opioid of first choice for moderate to severe pain.^{14,15} With dose titration a suitable level of analgesia can usually be achieved.¹⁵ For patients unable to take oral morphine, the preferred alternative route of administration for cancer pain is by continuous subcutaneous injection via a syringe driver.^{14,15} Subcutaneous infusion of diamorphine is the preferred choice for those patients requiring continuous parenteral opioids.^{15,16} Alternative opioids such

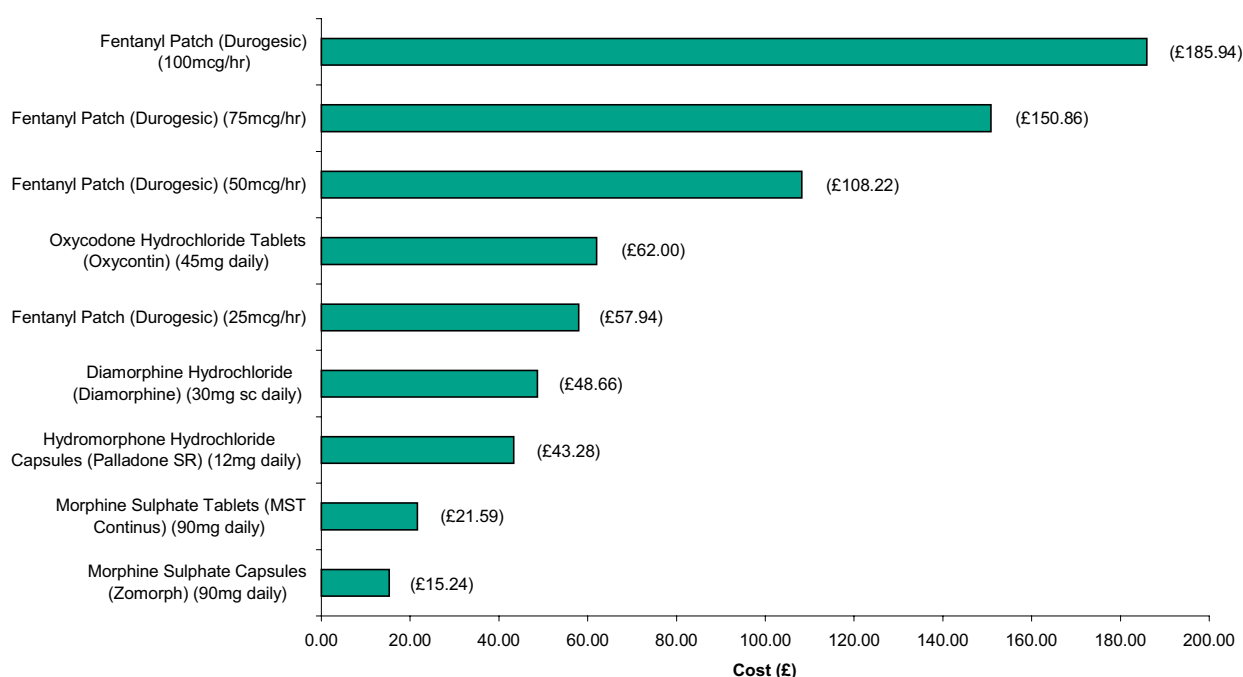
as oral hydromorphone and oxycodone can be considered for patients with persistent drowsiness and cognitive impairment associated with morphine.^{14,15} Methadone is another alternative but its use is generally reserved for specialist practitioners due to its complicated pharmacokinetics.¹⁴

When should it be used?

Fentanyl patches should be reserved for patients with stable pain who are already on a strong opioid and are unable to tolerate oral medications, as an alternative to subcutaneous administration.¹⁷ The patches do not allow for the flexibility required in patients with fluctuating pain or for titrating uncontrolled pain since the analgesic effects are not obtained until 12-24 hours after application of the patch.^{1,14} The manufacturer recommends waiting 24 hours before re-assessing pain control.¹

How much does it cost?

Cost for 30 days treatment (prices from MIMS/Drug Tariff June 2004)



N.B. Doses shown are for general comparison only and do not imply therapeutic equivalence

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KEY RCT - randomised controlled trial, CT-controlled trial, G-guidelines, O-open study, MA-meta analysis, R-review, U-unpublished, Abs- abstract, E-editorial

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