

DRUG UPDATE

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TRANSDERMAL BUPRENORPHINE

Transdermal buprenorphine is licensed for the treatment of moderate to severe cancer pain or severe pain unresponsive to non-opioid analgesics. In clinical trials involving patients with chronic pain it was not consistently superior to placebo. These trials did not distinguish between patients with cancer-related pain and other types of chronic pain. Transdermal buprenorphine has not been compared with other opioid analgesics or transdermal fentanyl. Comparative trials are needed before its clinical role can be established.

What is it?

Buprenorphine is an opioid analgesic administered sublingually or by injection for the treatment of moderate to severe pain. Transdermal buprenorphine (Transtec®, Napp Pharmaceuticals) is formulated as a matrix patch and is licensed for the treatment of moderate to severe cancer pain and severe pain not responding to non-opioid analgesics.¹

The patch is available in three strengths delivering 35, 52.5 or 70 mcg/hr over 72 hours.¹ The starting dose is determined by the dose and type of previous analgesic. Patients not previously taking an analgesic, or taking a non-opioid analgesic, should begin with a dose of 35 mcg/hr.¹ The patch should be replaced every 72 hours and at least 6 days should elapse before a new patch is applied to the same area of skin.¹ Sublingual buprenorphine should be available to treat breakthrough pain; if 0.4 - 0.6 mg/day is regularly required, the next patch strength should be used.¹

Blood levels of buprenorphine increase slowly after application of the first patch.¹ Therefore, additional analgesia may be required for the first 24-48 hours.

How effective is it?

Two double-blind placebo-controlled trials of transdermal buprenorphine have been published in full.^{2,3} Both trials included patients whose pain was controlled by other analgesics and dose adjustment of transdermal buprenorphine was not permitted. Sublingual buprenorphine was permitted as rescue analgesia. The primary endpoint in both studies was the response rate, defined as the proportion of patients who obtained at least satisfactory pain relief and who averaged 0.2

mg/day of sublingual buprenorphine.^{2,3}

The first trial included 151 patients with severe or very severe chronic pain (associated with cancer in 55%) who obtained at least satisfactory pain relief from 5 days pre-treatment with 0.8 - 1.2 mg/day sublingual buprenorphine.² Patients were then randomised to 9 days treatment with transdermal buprenorphine 35, 52.5 or 70 mcg/hr or placebo. There were no significant differences in the primary endpoint between placebo (31%) and any strength of transdermal buprenorphine (34%, 37% and 50% respectively) and there were also no significant differences in the use of rescue analgesia. Overall, more patients using transdermal buprenorphine reported good or complete pain relief, milder pain intensity and sleep uninterrupted for more than 6 hours by pain, but statistical significance was not reported.

In the second trial³, 154 patients with chronic severe pain (77% associated with cancer) were randomised to placebo or transdermal buprenorphine 35, 52.5 or 70 mcg/hr for up to 15 days. The response rate was significantly greater among patients using transdermal buprenorphine 35 or 52.5 mcg/hr (37% and 48% respectively), but not with the highest dose patch (33%) compared with placebo (16%). The mean daily dose of rescue analgesia was also significantly lower among all patients using transdermal buprenorphine (0.3 vs. 0.7 mg/day with placebo). According to mean pain relief scores recorded by patients, any strength of transdermal buprenorphine was superior to placebo (statistical significance not reported). More patients using the buprenorphine patch reported no or mild pain compared with placebo (46% - 61% vs. 41%) and fewer reported severe or very severe pain (8% - 17% vs. 24%). More patients reported sleep uninterrupted by pain for at least

6 hours with the buprenorphine patch (41% - 47% vs. 37%). Statistical significance was not reported for these endpoints.

The long-term use of transdermal buprenorphine has been reported in an open-label, uncontrolled follow-up study in 239 patients with moderate to severe chronic pain requiring treatment with an opioid (56% associated with cancer).⁴ The mean duration of use was 4.8 months. Pain control was rated as at least satisfactory by 90% of patients, of whom 42% rated it as good or complete.

How safe is it?

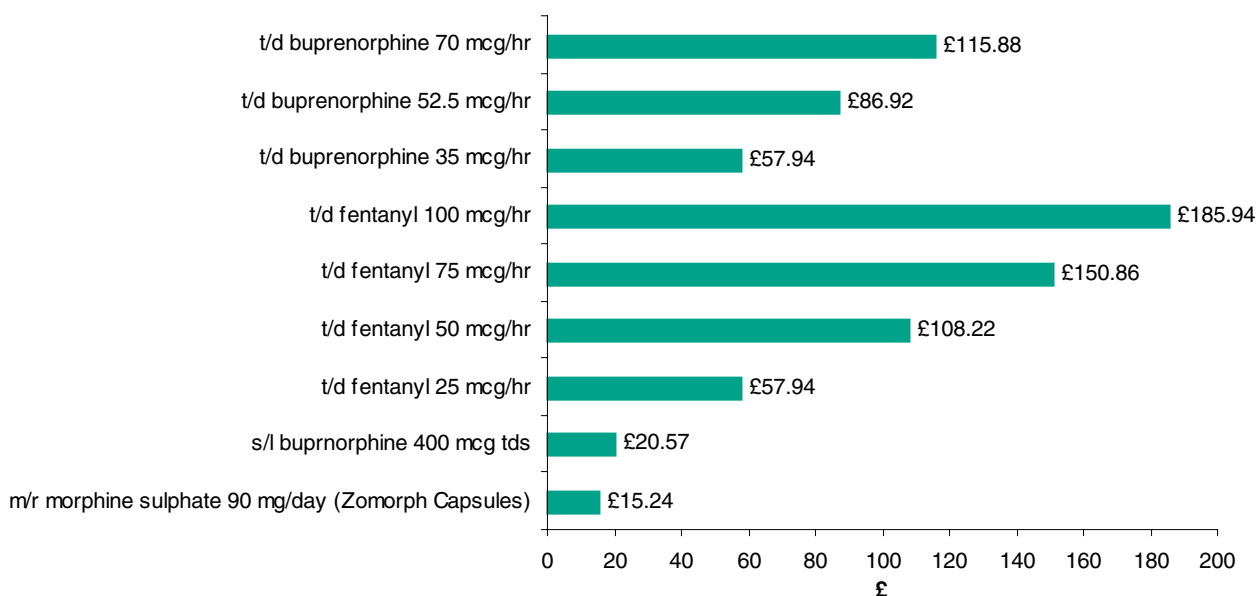
The commonest adverse events reported in clinical trials were nausea (17% of patients), erythema (17%), pruritus (15%), vomiting (9%), dizziness (7%), tiredness (6%) and constipation (5%).¹

When should it be used?

Transdermal analgesics offer limited advantages and should only be used in patients who have specific problems with oral therapy. They are not suitable for use in acute pain. Transdermal buprenorphine offers limited analgesic efficacy compared with placebo and efficacy has not been compared with other analgesics. A role in the clinical management of chronic pain has not yet been established.

How much does it cost?

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



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

REFERENCES

- 1 Transtec Summary of Product Characteristics. Napp Pharmaceuticals, 2002
- 2 Bohme K, Likar R. Efficacy and tolerability of a new opioid analgesic formulation, buprenorphine transdermal therapeutic system (TDS), in the treatment of patients with chronic pain. A randomised, double-blind, placebo-controlled study. *Pain Clinic* 2003;15:193-202 (RCT)
- 3 Sittl R, Griessinger N, Likar R. Analgesic efficacy and tolerability of transdermal buprenorphine in patients with inadequately controlled chronic pain related to cancer and other disorders: a multicenter, randomized, double-blind, placebo-controlled trial. *Clin Ther* 2003;25:150-68 (RCT)
- 4 Kopp M. Buprenorphine transdermal system (TDS) (delivery rate 35 mcg/h) in an open long-term study with chronic pain patients. *Pain in Europe III. Nice 2000 (abstr 260) (Abs)*

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

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