

**FAST FACTS AND CONCEPTS #268
LOW-DOSE BUPRENORPHINE PATCH FOR PAIN**

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Background Buprenorphine is an opioid agonist/antagonist that is used sublingually for opioid addiction treatment (see *Fast Fact #221*). In 2010, the Food and Drug Administration approved a buprenorphine transdermal system (the ‘Butrans®’ patch) for use in the United States. This *Fast Fact* reviews the use of buprenorphine for pain, with an emphasis on the new low-dose transdermal patch.

Pharmacology Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa- and delta-opioid receptors. It provides analgesia with decreased incidence of sedation, euphoria and respiratory depression compared to other opioids (1). A ceiling effect for pain relief, previously identified in animals and humans, has *not* been found at the lower doses used for analgesia. In doses available transdermally (up to 70 mcg/hour), buprenorphine does not antagonize the effect of other opioids used for breakthrough pain (2).

Equianalgesic Ratios Buprenorphine is effective parenterally for post-operative pain; 0.3 mg is equianalgesic to 10 mg IV morphine. A trial of sublingual buprenorphine for pain (an off-label use in the U.S.) found that 0.4 mg is as effective for acute pain as 5 mg IV morphine (3). The transdermal buprenorphine to oral morphine equianalgesic ratio has been reported to be between 1:70 to 1:115 (e.g., 100 mg of oral morphine/24 hours \approx 0.87-1.42 mg transdermal buprenorphine/24hr \approx 36-59 mcg/hr transdermal buprenorphine). The transdermal buprenorphine:fentanyl ratio is reported to be 0.8 mcg buprenorphine to 0.6 mcg fentanyl (4) (e.g., 20 mcg/hour of transdermal buprenorphine is approximately equivalent to 15 mcg/hour of transdermal fentanyl).

Using the Low-Dose Buprenorphine Patch The U.S. formulation of the buprenorphine transdermal system is recommended for opioid tolerant patients requiring up to 80 mg/day of oral morphine equivalents. The patch is available in strengths of 5, 10, and 20 mcg/hour, and is worn for seven days at a time. The 20 mcg/hour patch is not intended for initial use, but patients accustomed to the patch may be titrated to this dose. The safety and efficacy of transdermal buprenorphine has not been fully established in children. In children >13 years of age, the dosing is felt to be equivalent to adults. Buprenorphine reaches a steady state level 48 hours after application of the first patch, and, with a terminal half-life of 26 hours, levels decline slowly after patch removal. Withdrawal symptoms tend to be milder than with other long-acting opioids (5). Use of more than one patch at a time is not recommended due to risk of QT prolongation, with a mean QTc prolongation of 9.2 ms at a dose of 40 mcg/hour (6). **Note:** in Europe doses between 70-210 mcg/hour have been used for cancer pain with a different patch system (7).

Initiating the Low-Dose Buprenorphine Patch (Manufacturer’s Recommendations) (6)

Baseline Daily Oral Morphine Equivalent	Starting Patch Dose
<30 mg	5 mcg/hour
30-80 mg	10 mcg/hour
>80 mg/day	Usage not recommended

Clinical Applications The buprenorphine patch has shown to be non-inferior to other opioids in studies of chronic lower back pain, osteoarthritis, and cancer pain (8). Because of its kappa antagonism, it has theoretical advantages in the treatment of neuropathic pain, though evidence for this is limited to case reports (9, 10). It has also been shown experimentally to have antihyperalgesic effects (11). Other advantages of buprenorphine include a decreased risk of respiratory depression and a lack of accumulation in renal failure, including in hemodialysis patients (12). Some studies have reported less constipation, nausea, and sedation with buprenorphine (13,14). In a trial comparing transdermal

buprenorphine in patients over 65 with younger patients, older patients had equivalent analgesia without any differences in accumulation of buprenorphine or its metabolites (15).

Cost The average wholesale price (in 2015) for a month's supply of four 10 mcg patches is \$336.

Summary The low-dose transdermal buprenorphine patch is effective for mild to moderate chronic pain, both malignant and nonmalignant. However, given the dose limitations of the buprenorphine patch as marketed in the U.S., as well as the cost, the usefulness of this medication for most patients and clinicians is very limited. The low-dose buprenorphine patch may be a reasonable second- or third-line option in patients with low opioid requirements who experience intolerable side effects with other opioids.

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