BuTrans Patch

Buprenorphine Transdermal System (BTDS) for Weekly Application

**Classification**
- [Semisynthetic, highly lipophilic opioid; derivative of morphine](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- [Alkaloid thebaine; brain tissue levels for eucodal serum levels](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)

**Opioid analgesic (mu agonist; kappa & delta antagonist).** Narcotic and Controlled Drug (Canada).

It is often considered a partial mu agonist; however some recent literature suggests full potent mu activity. It's action may more resemble a full mu agonist at lower doses, and partial mu agonist at higher doses. 

**[Note](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/), a related product, SUBOXONE consists of [buprenorphine 2mg + naloxone an opioid antagonist 0.5mg](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/) as a SL tablet used to treat opioid dependence. Bioavailability of buprenorphine-variable: Transdermal ≥ 15%; SL= 30%-70%; Suboxone dosage range is 4-24mg/day buprenorphine. The amount of buprenorphine in 4 mg SL may equal to the amount in ≥10 BuTrans-20 patches. Only about 3% of the naloxone in Suboxone is absorbed; it will precipitate withdrawal if injected.**

**Strengths**
- [Patch (transderm.)](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- Persistent pain of moderate intensity in adults (≥20 kg) requiring continuous opioid analgesia for an extended period of time (not suitable for unstable or widely fluctuating pain).
- Can be used in opioid naïve patients (alternate to codeine, tramadol) and patients previously only on prn opioids.
- Considered when non-opioids provide inadequate relief and strong opioids undesirable in chronic non-cancer pain

**Use/Place in Therapy**
- [Initial BuTrans patch dose](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- [Oral Hydromorphone](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- [Oral Oxycodone](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- Acetaminophen + Codeine (30mg)

**Estimated Dose Equivalencies**

<table>
<thead>
<tr>
<th>Initial BuTrans patch dose if on previous opioid.</th>
<th>5 mcg/hr</th>
<th>5 mcg/hr</th>
<th>5-10 mcg/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimate of Eventual BuTrans® Patch Strength</td>
<td>$ 60</td>
<td>$ 105</td>
<td>$185</td>
</tr>
</tbody>
</table>

**Cost / 4 weeks:**
- 5mcg/hr: $ 60
- 10mcg/hr: $105
- 20mcg/hr: $185

**Contraindications (CI), official**
- Hypersensitivity, GI (ileus, surgical abdomen), mild/intermittent/acute pain, acute asthma/obstructive airway/respiratory depression, acute alcoholism/addiction, opioid dependence/acute opioid withdrawal, convulsive disorders, MAOIs within 14 days-myasthenia gravis, hepatic insufficiency, pregnancy/lactation; <40kg

**Dose**
- **(Patch provides sustained levels & analgesia over 7 days.)**
- **(High affinity for mu receptor = blockade may last >24hrs. Effect not totally related to plasma levels.)**

**Begin at:**
- [5 mcg/hr patch applied once weekly; titrate as necessary or](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- if previously on opioid (up to 80 mcg oral morphine equivalent/day) may start on 5-10mcg/hr patch once weekly (medication for breakthrough pain should also be provided).

**Dosage adjustments:**
- generally recommended after 2 days and not more frequently than after 3 days.

**Maximum dose:**
- 20mcg/hr.
- (Patch applied for 7 days.)
- Doses ≥40mcg/hr may be associated with QT prolongation (but less than methadone)

**Breakthrough pain:**
- may be managed by acetaminophen or NSAID +/- codeine or other breakthrough meds prn

**Adjustments:**
- Renal dysfx: NO dosage adjustment required; (hepatic metabolism glucuronidation & biliary excretion)

**Administration**
- Apply to: non-irritated, dry, intact skin; upper outer arm, upper chest, upper back or side of chest
- Do not apply creams or ointments to skin < 6 hours prior to patch application as may affect adhesion.
- If site irritation, consider a corticosteroid spray (e.g. beclomethasone or fluocinolone) to skin area prior to patch; (this lacks data & may affect absorption). (Alternately, steroid cream post-patch or well in advance (> 6-12hr) of patch application.)
- Rotate sites with each new patch; choose 4 or more sites and rotate; allow 3 weeks before reusing the same site
- Avoid exposure of patch to direct sunlight (∆↑ absorption). Showering, swimming & bathing should not affect patch.

**Drug Interactions (DI)**
- Metabolized via CYP3A4 to a metabolite.
- Other: Warfarin + INR= anesthetic, hepatic blood flow & buprenorphine; Benzodiazepines

**Adverse Events (AE)**
- [Common on initiation: nausea, dizziness, somnolence, constipation, pruritus, dry mouth](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)
- [Most are similar to other opioids.](https://www.rxfiles.ca/qanda/buprenorphine-transdermal-system-btds-weekly-application/)

**Discontinuing / Withdrawal**
- Consider tapering, if higher doses to reduce withdrawal symptoms; withdrawal generally mild & resolves in ≤2 weeks
- After removal of patch, levels decline gradually; ~ 50% ↓ over ~12 hours (10-24 hrs); administering a subsequent opioid after patch removal should generally be delayed until 24 hours after removal

**Other**
- Steady state levels in ~3 days. Heat sources (external: will ↑ absorption & risks; e.g. heat pad, hot bath, sauna, sunbathing, fever, etc.)
- Advantages: long-acting useful for chronic-stable type pain; once weekly application & kappa antagonist effect may result in less dysphoria, psychological craving & dependence (However, data from Norway suggests addiction concerns). May cause less withdrawal when stopped than other opioids; incidence of constipation may be lower.
- Compared to the fentanyl patch: lower abuse potential, mild withdrawal symptoms, may initiate in opioid naïve.
- Disadvantages: long & delayed action means it is not suitable for acute or fluctuating pain; adverse effects may be sustained for ≥24 hours after removal of patch. (If one holds that it is a partial mu agonist, this would limit the opioid effect resulting in both a ceiling dose & potential withdrawal in patients dependent on other long-term opioids). Studies are short term (e.g. s12 weeks; most ≤4 weeks); results modest & benefits ± harms (NNT = 7-8 & NNH for ↑AE = 6-9).

**Note however that opioid withdrawal may occur for patients taking long-term and/or higher doses of opioids after switching to buprenorphine!!**

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**Daily Opioid Dose** & Approximate Cost/4wks

<table>
<thead>
<tr>
<th>Acetaminophen + Codeine (30mg) ± Caffeine</th>
<th>≤6 (30mg) tabs</th>
<th>7-8 (30mg) tabs</th>
<th>$43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>≤100 mg</td>
<td>200 mg</td>
<td>$67</td>
</tr>
<tr>
<td>Tramadol</td>
<td>150 mg</td>
<td>300 mg</td>
<td>$100</td>
</tr>
<tr>
<td>Oral Morphine</td>
<td>≤15 mg</td>
<td>30 mg</td>
<td>$60</td>
</tr>
<tr>
<td>Oral Oxycodone</td>
<td>≤10 mg</td>
<td>15 – 20 mg</td>
<td>$64</td>
</tr>
<tr>
<td>Oral Hydrocodone</td>
<td>≤7.5 mg</td>
<td>12 – 15 mg</td>
<td>$72</td>
</tr>
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</table>

**Fentanyl Patch**
- 12 mcg/hr

**Note however that opioid withdrawal may occur for patients taking long-term and/or higher doses of opioids after switching to buprenorphine!!**

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**RxFiles Q&A Summary: Buprenorphine Transdermal Patch – Pg 1**
Table 1: Randomized controlled trials (RCT): buprenorphine transdermal system (BTDS) - BuTrans (7 day) patch, chronic non-cancer pain

<table>
<thead>
<tr>
<th>Patients</th>
<th>Intervention</th>
<th>Results (primary; other)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low back pain, mod-sev (VAS ≥25 for ≥5 weeks &amp; not well controlled: (most had long hx)</td>
<td>BTDs 5.10, 20mcg/hr vs Pl</td>
<td>VAS: 37.6 ± 20.7 vs 43.6 ± 21.2 (p&lt;0.01)</td>
<td>Exclusions: multiple (e.g. if expected to exceed max BTDS dose)</td>
</tr>
<tr>
<td>Axial pain: baseline pain: 62.1 ± 15.5</td>
<td>+ i ACC30 46.5 mg/day linker dose for BTDS</td>
<td>use of breakthrough tabs: 1.8 vs 2.4/day (NS)</td>
<td>79 patients enrolled; 53 patients evaluated per-protocol</td>
</tr>
<tr>
<td>PP: n=53 (203; 51)</td>
<td>+i crossover at 6wks</td>
<td>also improved: pain; sleep, disability, etc.</td>
<td>most patients (59%) titrated to highest dose (titrations weekly)</td>
</tr>
<tr>
<td>Baseline pain: 4.4 ± 1.0</td>
<td>Not ITT (only evaluated if ≥2 wys bck completed)</td>
<td>AE: &quot;severe&quot; as per patient/15% vs 42%</td>
<td>62% of patients chose to continue for 6 month open label follow-up where pain and QOL improvements were sustained</td>
</tr>
</tbody>
</table>

| Low back pain, mod-sev, on prior opioid (78 randomized) | BTDs 10.40, 200mcg/hr vs Pl | Mean dose = 29.6mcg/hr vs 32.5mcg/hr | Similar improvements in opioid & opioid naive patients |
| PP: n=53 (203; 51) | +i Acetaminophen 400mg prn | +i crossover at 6wks | | |
| Baseline pain: ≥4 (BS-11 on acetaminophen 4g/day) | No difference in pain disability index | | |

| Osteoarthritis (hip or knee); mod-sev | BTDs 10.5, 10, 20mcg/hr vs Pl | NS: 59 vs 73% (NNT=6; 95% CI: 1.39-4.95) | BTDS had modest benefit vs Pl considering prior opioid hx |
| PP: n=53 (203; 51) | +i Acetaminophen 500mg prn | +i crossover at 6wks | Some +ve 2 outcomes: e.g. get out of bed, sit in chair. |
| Baseline pain: ≥4 (BS-11 on acetaminophen 4g/day) | No significant difference | | 6mo follow-up open-label, 2740 completed +ve; limitations: not ITT, AE |

| Osteoarthritis (hip or knee); mod-sev | BTDs 10.150-400mcg/day vs Tramadol 150-400mcg/day | BS: 11 differenced scores: less nausea, vomiting & dizziness | 21 day run-in |
| PP: n=53 (203; 51) | +i Acetaminophen 500mg prn | +i crossover at 6wks | 6 severe adverse events: 1 fatal, not deemed related to BTDS; 1 hospitalization for biliary colic/spasm & 1 for hiccups & dizziness |
| Baseline pain: ≥4 (BS-11 on acetaminophen 4g/day) | No difference in BTDS & Pl in mean dose or titrations required | + patch site redness 50% & irritation 50%; some complaints of patch buckling or curling. |

Select Studies with different dose (e.g. 35-70mcg/hr) or dosage form (e.g. 3-4 day patch) than available in Canada: but of interest

| No pain complaints ≥2 months; on previous combination oral opioids | BTDs 10.5, 10, 20mcg/hr vs Pl, open-label (protocol) | No difference in pain disability index | 7 day run-on buprofen & inadequate relief on ibuprofen |
| PP: n=588 (~ at run-in;155% analyzed | +i Acetaminophen 500mg prn | +i crossover at 6wks | Artifical type of trial |
| Baseline pain: ≥4 (BS-11 on acetaminophen 4g/day) | No significant difference | + a number of ≥2 endpoints did not have significant differences but some "trends" supportive; | |
| n=427 actually randomized; right lateralized; (62%); age ~57 | | + subgroup: benefit only seen in knee subgroup, not hip | |

ACDs/acetaminophen/codeine/caffeine 30mg AE: adverse events BS-11=box score 11 point rating system CR=controlled release DB=double-blind ITT=intention to treat NNH=number needed to treat to harm one Opioids: morphine equivalent; not more than 750mg/24hr use of breakthru tabs: ≥1g/day (NS) NNT=number needed to treat to prevent one patient from having an adverse effect OR=odds ratio OX=placebo QOL=quality of life SGA=sublingual VAS=visual analogue scale

References

Prepared by Loren Regier. Sep 2010 (Update Dec/2011) for RxFiles Academic Detailing. www.RxFiles.ca. Thanks to the many reviewers who provided input.

Additional References and Links


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1 CPS 2010 Product Monograph - BuTrans
5 ACC30=acetaminophen/caffeine/codeine 30mg  AE=adverse events  BS-11=box score 11 point rating system  CR=controlled release  DB=double-blind  ITT=intention to treat  NNH=number needed to treat to harm one
Comments (anecdotal) from clinicians on switching from other opioids to BuTrans

- Officially not recommended in Canada, but some experience has been positive
- Limited experience; if done, most success with tapering down the other opioids prior to switch to Butrans 5 or 10 and then titrated up as necessary. Direct opioid rotations mostly only for doses <40-60 mg/day of morphine.
- Encourage non-drug therapy complementary approaches in addition to drug therapy; essential for long term success of CNCP
- Relative potency for switching is not well established:
  - BuTrans 5 = .12 mg/day ≈ 10 mg/day morphine or 7.5 mg/day oxycodone
  - BuTrans 10 = .24 mg/day ≈ 20 mg/day morphine or 15 mg/day oxycodone
  - BuTrans 20 = .48 mg/day ≈ 40 mg/day morphine or 30 mg/day oxycodone
- Example- pt on 40 mg morphine (Meslon 20mg bid) with poor pain relief (VAS 8/10)
  - Option #1 (preferred?) Wean patient down to 20mg/day (10 mg am 15mg pm X 1-2 weeks the 15mg BID X 1-2 weeks the 10 mg am 15mg pm X 1-2 weeks then Sat am take last does of 10mg M-Eslon and apply BuTrans 10mg patch. Use MS-IR 5 mg bid pm for any withdrawal or severe pain
  - Option 2 = Patient on 20 mg M-Eslon bid; Sat am apply BuTrans 20 patch and take last dose of 20mg M-Eslon. Then use MS-IR 5-7.5 mg bid-tid severe pain or withdrawal.
  [MS-IR = immediate release morphine sulphate]