TRANSDERMAL OPIOID PATCHES
(Fentanyl and Buprenorphine)
Dosing, Administration and Monitoring Guidelines

Guideline purpose and related documents

To provide guidance on the dosing, administration, management and monitoring of patients prescribed transdermal opioid patches (Fentanyl or Buprenorphine) for the treatment of chronic pain.


Points to consider when prescribing and using the Transdermal Opioid Patches

Transdermal Fentanyl Patch:
• Fentanyl is a potent opioid analgesic. Transdermal Fentanyl patches are unsuitable for opioid naïve patients (1).
• Until plasma concentrations are therapeutic (18-24hrs) breakthrough analgesia should be offered (2).

Transdermal Buprenorphine Patch:
• Buprenorphine is a less potent opioid than Fentanyl. Consider use when oral opioids such as codeine and tramadol are ineffective, or a more convenient alternative is required. The 5microg/hr patch may be initiated in opioid naïve patients (3).
• Until plasma concentrations are therapeutic (3 days) breakthrough analgesia should be offered.

Pharmacokinetics and Pharmacodynamics

Fentanyl is rapidly and primarily metabolised in the liver via CYP 3A4 enzyme and has no active metabolite. It takes 18 - 24 hours to reach therapeutic plasma concentrations, and a peak serum concentration 24 - 72hours after the first application (2).

Buprenorphine is metabolised in the liver via CYP3A4 enzyme. It is mainly excreted unchanged in the faeces. The half-live is 20-36hrs after transdermal use. Buprenorphine takes 3 days to reach steady plasma concentrations (3, 11).

Mechanism of Action and Indications

• Fentanyl is an opioid agonist at mu-opioid receptors in the human brain, spinal cord and other tissues (2).
• Buprenorphine is a partial opioid agonist at mu-opioid receptors in the human brain, spinal cord and other tissues (3).

Buprenorphine’s opioid agonist effect is dose related, however a ceiling effect to analgesia has been documented. Buprenorphine also has opioid antagonistic activity which may precipitate an abstinence syndrome in patients who are physically dependent on opioid agonists, depending on the level of dependence, timing and dose of buprenorphine (3).

Indications for transdermal opioid patches include the management of moderate to severe chronic pain requiring analgesia, and an alternative to morphine for patients with established opioid needs. They are a suitable choice if there is/ are:
1. Stable pain
2. Inability to take / poor absorption of oral medications or poor compliance with oral medications
3. Presence of significant renal impairment (fentanyl and buprenorphine have insignificant renal excretion) (1)
4. Unacceptable side effects with other opioids.

Contraindications

Fentanyl
• Hypersensitivity to any component of Fentanyl transdermal patch
• Opioid naïve patient with non-cancer pain (high rate of adverse effects)
• Acute, postoperative or intermittent pain (2)
• Patients concurrently receiving nonselective MAOIs, or within 14 days of stopping MAOI treatment
**Buprenorphine**

- Hypersensitivity to any component of Buprenorphine Transdermal Patch
- Myasthenia gravis
- Delirium tremens
- Severely impaired respiratory function
- Transdermal Patches are NOT indicated for the treatment of opioid dependence and opioid withdrawal (3)

**Precautions**

When converting from one opioid analgesic to another, overestimating can result in fatal overdose with the first dose – consult the Acute Pain Service, Equianalgesic dosing charts in eTherapeutic Guidelines or Product Information (MIMS).

**Fentanyl and Buprenorphine Transdermal Opioid Patches (2, 3)**

- Respiratory Depression and Sedation - Patients should be monitored – see monitoring.
- Patients with a history of drug or alcohol dependence
- Hepatic Impairment
- Accidental exposure by patch transfer to the skin of non-patch wearer may result in an opioid overdose for the non-patch wearer. If accidental transfer occurs, remove immediately.
- Head injuries and increased intracranial pressure
- Patients undertaking radiotherapy – do not commence Transdermal Opioid Patches (an existing regimen may continue)
- Thin and Emaciated patients - may experience reduced absorption, as fatty tissue is required for better absorption.
- Elderly patients are particularly susceptible to adverse effects - monitor closely and titrate the dose accordingly.
- **Buprenorphine** may lower the seizure threshold in patient with a history of seizure disorder (3).
- QTc Interval prolongation - High doses of **Buprenorphine** (40microg/hr) may prolong the QTc interval (3).
- Avoid direct exposure to external heat sources (e.g. Hot pack/ electric blanket/ hot water bottle) - may increase the release and absorption of the opioid. Bathing in hot water if allowed as patch is waterproof (avoid prolonged exposure)

**Dosage**

When it comes to dose titration remember to ‘start low and go slow’ (1).

**Fentanyl Transdermal Patches**

- Fentanyl Transdermal patches should be changed every 72 hours (Note: 25% of patients have larger breakthrough medication requirements on the 3rd day after patch application and may require a change every 48 hours [1])
- Dose should be titrated initially to ≤25 microg/hr Fentanyl, then titrate the dose up/down by 12 to 25 microg/hr
- Initial evaluation of the analgesic effect should not be made before the patch has been worn for 24 hours
- If the patient has previously been on opioids refer to the table below for a guide for conversion equivalent [adapted from eTherapeutic Guidelines: Palliative Care 2012 (1)]. Consult Palliative Care/Pain Service when converting between opioids.

<table>
<thead>
<tr>
<th>Patch strength (mg)</th>
<th>Delivery rate(micrograms/hour)</th>
<th>Parenteral morphine dose equivalent (mg/24hours)</th>
<th>Oral morphine dose equivalent (mg/24hours)</th>
</tr>
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<tbody>
<tr>
<td>2.1</td>
<td>12</td>
<td>15 - 30</td>
<td>30 - 60</td>
</tr>
<tr>
<td>4.2</td>
<td>25</td>
<td>30 – 40</td>
<td>60 – 100</td>
</tr>
<tr>
<td>8.4</td>
<td>50</td>
<td>60 – 80</td>
<td>120 – 200</td>
</tr>
<tr>
<td>12.6</td>
<td>75</td>
<td>90 – 120</td>
<td>180 – 300</td>
</tr>
<tr>
<td>16.8</td>
<td>100</td>
<td>120 – 160</td>
<td>240 – 400</td>
</tr>
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</table>

**Discontinuation:** Do not discontinue abruptly. Gradually downward titrate the dose every 3 days to prevent withdrawal in the physically dependent patient. Consider introducing an immediate release opioid medication if needed. An alternative opioid should not be administered within 24 hours of removal of the patch as fentanyl serum concentrations decrease gradually, and the analgesic effect is maintained for 24 hours after patch removal (1).
Buprenorphine Transdermal Patches

• Buprenorphine Transdermal patches provide 7 days continuous analgesia and should be changed every 7 days
• The lowest strength of the Buprenorphine Transdermal Patch (5microg/hour) should be used as the initial dose in opioid naive patients and in those converting from other opioids or fixed ratio opioid/ non-opioid combination drugs.
• Buprenorphine patches have been used as an alternative in patients taking lower doses of opioids (up to 90 mg of oral morphine equivalents a day) and combination analgesics. Such patients should be started on a low dose of Buprenorphine patch and continue with the same dose and dosing scheduling of their previous daily regimen during titration (3).
• If necessary, titrate the dose upwards in 5-10microg/hr increments to relieve pain and improve function, no less than every 3-7days which is when steady state levels are achieved.
• Maximum dose is 40 microg/hr (2x20microg/hr patches). (Maximum 20microg/hr unless under specialist advice) (3).

Discontinuation: Do not discontinue abruptly. Gradually downward titrate the dose every 7 days to prevent withdrawal in the physically dependent patient. Consider introducing an immediate release opioid medication if needed. An alternative opioid should not be administered within 24 hours of removal of the patch as buprenorphine serum concentrations decrease gradually, and the analgesic effect is maintained for 24hours after patch removal (3).

Administration

• Transdermal Opioid patches should not be cut nor divided. Damaged patches should not be used (2,3).

Application and Disposal of the Transdermal Opioid Patches

Following the correct checking procedure, the following method of application is advised:

1. Identify a clean, intact, hairless, preferably flat, non-inflamed, non-lymphoedematous area of skin on the upper torso below the neck and above the waist (clip hair if required, do not shave)
2. Wash and dry the skin with water only and do not apply lotions, oils or creams (may cause poor adhesion to the skin)
3. Wash the hands with water only and dry them immediately before the application of the patch (usual hand hygiene practices consistent with infection control policy should still be adhered to before and after patient contact)
4. Open the sachet containing the patch ensuring the integrity of the patch. Remove the backing on the patch. Do not cut or fold the patch during its application.
5. Apply the patch to the selected skin area and press firmly for 30 seconds to ensure adherence.
6. Record the date and time of application on the patch.
7. The nurse applying new patch is responsible for the removal of the old patch and recording application on the drug chart.
8. The patch should be checked every nursing shift for integrity and adhesion with documentation in the medical record.
   • Patches may be poorly adherent if the skin is hairy, oily, exposed to water or sweating.
   • If the edges of the patch loosen from skin, skin tape may be applied to the edges of the patch only (2-4, 8).
   • If adhesion problems persist, the patch may be overlaid with a waterproof or semipermeable adhesive dressing that may be worn until the patch is due to be replaced, such as Tegaderm® (2-4, 6-8).
8. In a patch falls off, dispose of it in a sharps bin as per Schedule 8 destruction in Medicines Policy. Apply a new patch.
9. Block out non-administration days on the medication chart
10. Record the site of application on the medication chart
11. The site of application needs to be rotated to protect the skin and ensure optimal absorption.
12. When changing the patch – remove from patient’s skin, fold it over on itself and discard into a sharps bin, to prevent retrieval and abuse. See Medicines Policy 14 - Drugs of Dependence: Schedule 8/ Schedule 11 Medication Management.

Common Adverse Effects

• Note: if a patient experiences any serious adverse effects, monitor them closely for 24-48 hours after patch removal as the serum concentration declines gradually (Fentanyl’s terminal half-life is 25hrs and buprenorphine’s is 36hrs) (11).
   Sedation and impaired cognition – warn patients not to drive until effects on cognition have stabilised (1).
• Respiratory depression (respiratory rate (RR) reduction is an unreliable indicator of respiratory depression (high blood CO₂ levels) which can coexist with a normal RR. Sedation is a more sensitive indicator of respiratory depression (1).
• Nausea, vomiting, hallucinations, sweating, urinary retention, skin reactions, tolerance, physical dependence, addiction
• Constipation (always co-prescribe laxatives with long-term opioids and advise patient to use according to need)
Drug Interactions (2, 3, 9)

- **Central nervous system depressants**: may produce additive effects. Respiratory depression, hypotension, profound sedation or coma may occur.

- **Serotonergic drugs, Monoamine oxidase inhibitors (MAOI), or within 14 days of stopping a MAOI**: Concomitant administration of **Fentanyl** is not recommended as serotonin syndrome may occur (9).

- **CYP3A4 inhibitors/Inducers** - Fentanyl and buprenorphine are metabolised via the CYP3A4 enzyme. Buprenorphine also inhibits CYP3A4. Concomitant use of **CYP3A4 inhibitors** (e.g. ritonavir, indinavir, neflinavir, ketoconazole, itraconazole, clarithromycin, verapamil, diltiazem, amiodarone) may increase fentanyl or buprenorphine plasma concentrations which may cause toxicity. Concomitant use is not recommended unless the patient is closely monitored.

Concomitant use with **CYP3A4 inducers** (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin, St Johns Wort) may lead to increased clearance and reduced analgesic efficacy. Monitor and increase dose if necessary.

Monitoring

- **Respiratory Depression** - A decrease in respiratory rate is a very unreliable indicator of respiratory depression (high blood carbon dioxide levels), which can coexist with a normal respiratory rate. **Sedation** is a more sensitive indicator of respiratory depression (1). The **Respiratory rate** should be monitored on the Adult Observation and Response Chart.

- **Impaired Cognition and Sedation** – Sedation score should be monitored on the Adult Observation and Response Chart.

- **Liver function tests** should be checked before and monitored throughout therapy with Buprenorphine.

Monitor carefully when used in the following circumstances (safety has not been established):

- Patients under 18 years and over 70 years
- Patients weighing less than 50 kg
- Febrile patients (over 40 °C) may increase opioid absorption monitor for side effects and adjust the dose if necessary.

Overdose

- **Symptoms**: Respiratory depression, apnoea, sedation/drowsiness, cardiovascular collapse, marked miosis.

- **Treatment**: Remove any patch in contact with the patient and call a MET code as a patent airway may need to be established. Oxygen, intravenous fluids, vaspressors/other supportive measures should be employed as indicated.

  The opioid antagonist **Naloxone** may reverse the effects of opioids. Dispose of the patch in a sharps container as per SVHM Medicines Policy 14 - Drugs of Dependence: Schedule 8/ Schedule 11 Medication Management.

Pregnancy and Breastfeeding (10)

**Fentanyl** - is considered safe to use in pregnant and breastfeeding women however there is more experience with slow release oral opioids such as morphine. Consult Medicines Information for more details (ext 4359).

**Buprenorphine** - The manufacturer contraindicates the use of the patches for analgesia during pregnancy however the buprenorphine film/sublingual tablets have been used to treat opioid dependence. Consult Medicines information (ext 4359).

Logistic Considerations

- Transdermal Opioid patches are located in the S8 Safe and will be imprest stock for some general medicine/rehab wards.

- **After Hours Supply** – If patches are not on imprest, they may be transferred from another ward that has imprest stock.

Presentation and Storage

- **Fentanyl Transdermal Patches (Durogesic® or Fentanyl Sandoz ®)** Strengths available at SVHM:
  - 12 microg/hour Patch (contains 2.1mg Fentanyl)
  - 50 microg/hour (contains 8.4mg Fentanyl)
  - 100 microg/hour (contains 16.8mg Fentanyl)
  - Store patches in the unopened pouch below 30°C (2).

- **Buprenorphine (Norspan®)** Strengths available at SVHM:
  - Buprenorphine patch releasing 5 microg/hour
  - Buprenorphine patch releasing 10 microg/hour
  - Buprenorphine patch releasing 20 microg/hour
  - Store patches in the unopened pouch below 25°C (3).
REFERENCES
6. Micromedex.com, Buprenorphine Transdermal, Truven Health Analytics Inc. 2015, accessed online on 18/08/15 at www.micromedexsolutions.com
7. Micromedex.com, Fentanyl Transdermal route, Truven Health Analytics Inc. 2015, accessed online at on 18/08/15 at www.micromedexsolutions.com
8. Lexicomp, Buprenorphine: Drug Information Lexicomp(R), in Topic 9170 Version 145.02015, UptoDate(R).

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