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# 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.

**Related Documents**:

- Medicines Policy 14 - Drugs of Dependence - S8 and S4D Medication Management
- Guideline for Opioid Analgesic use in the Acute Setting (Appendix 1 – Restrictions)

### Points to consider when prescribing and using the Transdermal Opioid Patches

**Transdermal Fentanyl Patch:**

- Fentanyl is a **potent** opioid analgesic, **~100 fold** more potent than morphine. Transdermal Fentanyl patches are **unsuitable for opioid naïve patients** [1].
- Breakthrough analgesia should be offered until plasma concentrations have reached steady state (18 to 24, up to 72 hours) , and following this, on a 'PRN' - when required- basis[2].

**Transdermal Buprenorphine Patch:**

- Buprenorphine is a **less potent** opioid than Fentanyl, and **~75 fold** more potent than morphine. The 5 microg/hour patch may be initiated in opioid naïve patients [3].
- Breakthrough analgesia should be offered until plasma concentrations have reached steady state (72 hours) and following this, on a 'PRN' - when required- basis.

Prescribers should annotate the Medication chart with **'remove old patch'** when prescribing Opioid Patches, (see **Administration**) to reduce the risk of opioid toxicity from 2 patches unintentionally being in place at once.

### Pharmacokinetics and Pharmacodynamics

**Fentanyl** is rapidly and primarily metabolised in the liver via CYP 3A4 enzymes and has no active metabolite. It takes 18 to 24 hours to reach steady state plasma concentrations, and a peak serum concentration 24 to 72 hours after the first application [2].
**Buprenorphine** is metabolised in the liver via CYP3A4 enzymes. It is mainly excreted unchanged in the faeces. The half-life is 20 to 36 hours 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 and opioid requirements**
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

**Transdermal opioid patches are unsuitable for the management of acute pain given the slow onset and offset. Rapid and safe dose titration is not possible [12]**

**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,** or other specialty pain team, and **ANZCA FPM Opioid Calculator App for smartphones, eTG, or Product Information (MIMS)**. Note that the Safer Care Victoria Opioid Conversion Guidance document is also available but is not as detailed as these references. For staff unfamiliar with converting opioids, reference to the eTG, ANZCA FPM app and MIMS-PI is recommended.

**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 – avoid applying patch to irradiated skin due to increased erythema. Apply to non-irradiated skin.
- 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.
- May lower the seizure threshold in patient with a history of seizure disorder or risk factors for seizures [3].
- QTc Interval prolongation - High doses of **Buprenorphine** (40 microg/hour) 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 is allowed as patch is waterproof (avoid prolonged exposure)

## Dosage

**When it comes to dose titration remember to 'start low and go slow' [1].**

**Consult or refer to the APS or Palliative care Team if there is any uncertainty regarding changing opioids, calculating equianalgesic doses, or prescribing breakthrough analgesia.**

**Fentanyl Transdermal Patches** [1]

**When changing from another opioid to Fentanyl, or changing the route of administration:**

- When changing from one opioid to another opioid, the new opioid is usually started at 50 to 75% of the calculated equianalgesic dose and any shortfall in pain relief is managed with breakthrough doses until the patch is therapeutic (18 to 24 hours for Fentanyl).
- Consider using the lower dose (i.e. 50% of the calculated equianalgesic dose) for older and/or frail patients, or when changing from very high opioid doses (e.g. more than oral morphine 100 mg [or equivalent] in 24 hours).

1. Calculate the **total amount of opioid taken in the previous 24 hours** (i.e. include regular and breakthrough doses of all opioids, **except** doses taken for incident pain).
2. Convert this to an **oral morphine equivalent daily dose** (equivalent dose of oral morphine that would need to be taken over 24 hours), and then convert this to the **appropriate dose for the Fentanyl patch.**
   These can both be done using either:
   - ANZCA FPM Opioid Calculator App for smartphones (***Recommended*** – this includes a recommended dose that is equivalent to a 25 to 50% reduction in dose, which is usually required due to tolerance of the opioid)
   - Approximate equianalgesic doses of opioids from Table 1.27 of the Pain and Analgesia eTherapeutic Guidelines (eTG).
     i. See Box 10.29 of the Palliative Care eTG for an example of how to calculate an approximate equianalgesic dose when changing from one oral opioid to a different oral opioid.
     ii. Box 10.27 of the Palliative Care eTG describes how to calculate an approximate equianalgesic dose when changing from an oral opioid to a transdermal patch, and Box 10.28 of the Palliative Care eTG shows an example of a dose calculation.
   - Tables giving suggested starting doses in the **Fentanyl patch Product Information** (PI -MIMS) Note: the equianalgesic ratios used in the **Fentanyl patch PI** have been shown to be sufficiently conservative such that t**he usual additional reduction** in the calculated equianalgesic dose (25 to 50%) is **not required**.[(1)]
3. **Confirm with a specialty pain service physician that the calculated equivalent strength of opioid patch is correct**.
4. Prescribe a 'PRN' dose of immediate-release opioid to treat **breakthrough pain** (normally one-twelfth to one-sixth of the oral morphine equivalent daily dose, when required). This is required until the patch becomes therapeutic. Box 10.27 of the Palliative Care eTG also describes how to calculate a dose of opioid for breakthrough pain for a patient using a transdermal fentanyl patch.
5. Consult Table 10.5 of the Palliative Care eTG OR Safer Care Victoria Guidance on Opioid Conversion – 14. Timing a change of opioid formulation and/or route of administration (same), for suggestions on how to time changing an opioid formulation /route of administration in palliative care if changing to/from a patch.

- Initial **evaluation of the analgesic effect** should not be made before the patch has been worn for 24 hours
- Dose should be titrated initially to ≤25 microg/hour Fentanyl, then titrate the dose up/down by 12 to 25 microg/hour every 72 hours
- **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. If this occurs, **consider whether an alternative analgesic may be a more suitable for the patient. Consult a specialty pain** service if unsure. Some patients may require a patch change every 48 hours [(1)], although this should only be prescribed by a specialty pain service.

**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 slow release 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

- The lowest strength of the Buprenorphine Transdermal Patch (**5 microg/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 are an alternative in patients taking **lower doses of opioids** (up to 90 mg of oral morphine equivalent daily dose) and combination analgesics. **Such patients should be started on a low dose of Buprenorphine patch**

**and continue taking the same dose and dosing scheduling of their previous daily regimen during titration** (72 hours until steady state is obtained). [3]

- If necessary, titrate the dose upwards in 5 to 10 microg/hour increments to relieve pain and improve function, no less than every 3 to 7 days which is when steady state levels are achieved.
- Max 20microg/hour unless under specialist advice [3]. **Maximum dose is 40 microg/hour**.
- **Buprenorphine Transdermal patches provide 7 days continuous analgesia, and should be changed every 7 days.**

**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 24 hours after patch removal [3].

## Administration

- **Transdermal Opioid patches should not be cut or 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, and the **date and time for removal on the patch**.
7. The nurse applying the new patch is responsible for **removing** the old patch and **recording** the application on the drug chart.
8. 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 4D Medication Management**.
9. **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].
   - In a patch falls off, dispose of it in a sharps bin as per **Schedule 8 destruction in Medicines Policy 14 - Drugs of Dependence: Schedule 8/ Schedule 4D Medication Management**. Apply a new patch.
10. Block out non-administration days on the medication chart, and draw a square around the day that patch administration is due. **Annotate the medication chart with 'Remove old Patch' under the day the patch is due to be changed (see prescribing example below).**
11. **Record the site of application on the medication chart (either in the date and month or pharmacy section – see prescribing example below).**
12. The site of application needs to be rotated to protect the skin and ensure optimal absorption.

## Prescribing Example

**REGULAR MEDICATIONS**

YEAR 20 22 — DATE & MONTH →
DOCTORS MUST ENTER administration times

| Date | Medication (Print Generic Name) | Tick if Slow release | 7/6 | 8/6 | 9/6 | 10/6 | 11/6 | 12/6 | 13/6 | 14/6 | 15/6 | 16/6 | 17/6 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7/6 | Fentanyl Patch | | | | Left arm | | | | | | | | |
| Route | Dose — Frequency & NOW enter times | 0800 | X | X | ✓ | X | X | | X | X | | X | X |
| Top | 50microg/hr every 72 hours | | | | Remove old patch | | | Remove old patch | | | Remove old patch | | |
| Indication: Pain | Pharmacy: A. Pharmacist | | | | | | | | | | | | |
| Prescriber Signature: A. Doctor | Print Your Name: A. Doctor | Contact: #311 | | | | | | | | | | | |

Continue on discharge? Yes / No
Dispense? Yes / No
Duration? ..... days/Qty? .....
Date .....

## Common Adverse Effects

- Note: if a patient experiences any **serious adverse effects**, monitor them closely for 24 to 48 hours after patch removal as the serum concentration declines gradually (Fentanyl's terminal half-life is 25 hours and buprenorphine's is 36 hours) [11].
- Sedation and impaired cognition: warn patients not to drive until effects on cognition have stabilised [1].
- Respiratory depression. Note that respiratory rate (RR) reduction is an unreliable indicator of respiratory depression - high blood $CO_2$ levels 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.

## Interactions [2, 3, 9]

- As the opioid patches may maintain therapeutic levels for days after removal, drug interactions may persist until the levels are below therapeutic. Elimination takes 5 half-lives. Fentanyl patches have a half-life of 20 to 27 hours. Buprenorphine is also partial opioid agonist, so may also **block** the therapeutic effect of other opioids to some degree, for up to 5 half-lives after patch removal (Buprenorphine's half-life ranges from 24 to 48 hours) [6,7].
- **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, nelfinavir, 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 John's 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 (SV978).
- **Impaired Cognition and Sedation** – Sedation score should be monitored on the Adult Observation and Response Chart (SV978).
- **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, vasopressors/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 4D Medication Management**.

## Pregnancy and Breastfeeding [10]

**Fentanyl** - is considered safe to use in pregnant and breastfeeding women at the lowest effective dose for the shortest duration possible, however there is more experience with slow release oral opioids such as morphine. Monitoring and management of the neonate is required following regular use in the third trimester, and if breastfeeding. Consult Medicines Information (ext 4359).
**Buprenorphine** - is considered safe to use in pregnant and breastfeeding women at the lowest effective dose for the shortest duration possible, however there is more experience with slow release oral opioids such as morphine. Monitoring of the neonate is required following regular use in the third trimester, and if breastfeeding. 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 (contains 2.1mg Fentanyl)
  - **25** microg/hour (contains 4.2mg Fentanyl)
  - **50** microg/hour (contains 8.4mg Fentanyl)
  - **75** microg/hour (contains 12.6mg Fentanyl)
  - **100** microg/hour (contains 16.8mg Fentanyl)
  - Store patches in the unopened pouch below 30ºC [2].
- **Buprenorphine (Norspan®) Strengths available at SVHM:**
  - Buprenorphine patch releasing **5** microg/hour
  - Buprenorphine patch releasing **10** microg/hour
  - Buprenorphine patch releasing **15** microg/hour
  - Buprenorphine patch releasing **20** microg/hour
  - Buprenorphine patch releasing **25** microg/hour
  - Buprenorphine patch releasing **30** microg/hour
  - Buprenorphine patch releasing **40** microg/hour
  - Store patches in the unopened pouch below 25ºC [3].

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