

FACTSHEET 5 ON PALLIATIVE CARE THE USE OF TRANSDERMAL OPIOIDS – FENTANYL AND BUPRENORPHINE ‘PATCHES’

Transdermal administration is an alternative (not necessarily ‘better’) method of drug administration. NICE recommends that oral sustained-release morphine is prescribed as first-line maintenance treatment where strong opioids are required.

Following application of a ‘patch’ there is a delay of many hours before therapeutic levels of the drug are achieved. Similarly, after removing a patch, there is a delay of many hours before circulating levels of drug drop to sub-therapeutic level.

i.e. there is a SLOW ONSET and SLOW OFFSET of analgesia and there is a SLOW ONSET and SLOW OFFSET of side effects

ACUTE PAIN IS AN ABSOLUTE CONTRA-INDICATION FOR USE OF TRANSDERMAL ROUTE

Situations where it MAY be appropriate to use transdermal opioid patches:

- | | |
|---|--|
| 1. Dysphagia | Developing in patients with known opioid requirements, unable to tolerate other morphine formulations e.g. solution, suspension. |
| 2. Inability to swallow | e.g. neurological disorders MND/post CVA where prolonged alternative parenteral/enteral administration is inappropriate. |
| 3. Poor absorption | e.g. short bowel/inflammatory bowel disease. |
| 4. Vomiting | Where patient’s condition is otherwise stable but unpredictable vomiting causes unpredictable absorption. |
| 5. Uncompliant Patient | In the community where it is not possible to ensure regular oral administration. |
| 6. Persistent excessive drowsiness/side-effects | From other opioids, occasionally benefit from conversion to transdermal opioid e.g. constipation may be less |
| 7. Haematological disorders | When oral route unavailable and subcutaneous route to be avoided (causes haemorrhage/bruising) |

- **OPIOIDS should be used with great caution in chronic pulmonary disease**

CONTRA-INDICATIONS/PRECAUTIONS

- Patch must be applied to healthy skin. In patients where patch fails to adhere **DISCONTINUE USE**
- **AVOID** use in patients with known hypersensitivity i.e. to fentanyl, buprenorphine or the adhesive system.
- **TEMPERATURE INCREASE** (fever, bath, heat pad) may increase delivery rate causing toxicity and shortening duration of action of patch.
- **TOXICITY** - is more likely in the elderly or those with co-morbidities
 - respiratory depression
 - drowsiness/diminished level consciousness
 - twitching (myoclonic jerks)

PATCH APPLICATION

Instructions for the use and application of patches accompany all prescriptions, general principles include:

- Apply patch to an area of hair free skin, preferably on the upper torso in an area that is relatively flat and therefore allows for good contact and application.
- Avoid skin that is red, irritated or otherwise flawed.
- The area of application should be clean, dry and cool. Soap should not be used to wash the area immediately prior to application, neither should creams or lotions be applied to the area of application.
- Replacement patches should be sited in an area distant from previous patch.

BUPRENORPHINE

Buprenorphine is a synthetic opioid. It binds at opioid receptors and produces analgesia through mu-receptor agonist properties. Thus its side effect profile is similar to morphine and other opioids. At recommended doses the 'ceiling' effect for analgesia is not reached.

Transdermal patches containing buprenorphine are licensed for moderate to severe cancer pain and severe pain unresponsive to non- opioid analgesics.

'BUTRANS'

Buprenorphine "low dose" patches are applied for 7 days and changed on a weekly basis. There are 3 strengths, 5 microgram per hour (equivalent to oral codeine 60mg per day); 10mcg per hour (equivalent to oral codeine up to 120mg per day); 20 microgram per hour (equivalent to oral codeine up to 180mg per day). Due to the low dose side effects are likely to be proportionately lower.

‘TRANSTEC’

Buprenorphine patches are available in 3 strengths; 35 microgram/hr, 52.5 microgram/hr and 70 microgram/hr respectively, corresponding to a daily dose of 0.8mg, 1.2mg and 1.6mg buprenorphine. All patches are for 96 hour (4 days) application.

The 35microgram/hr patch is equivalent to 30 to 60mg oral morphine in 24hrs. Maximum recommended 2 x 70microgram/hr is equivalent to 240mg morphine per 24hrs.

Taken from British Pain Society *Opioids for Persistent Pain - January 2010*

Transdermal opioids: Approximate equivalence with oral morphine										
Oral morphine equivalent (mg/24 hours)	10	15	30	45	60	90	120	180	270	360
Transdermal buprenorphine (microgram/hr)	5	10	20		35	52.5	70			
Transdermal fentanyl (microgram/hr)				12		25		50	75	100

- Therapeutic levels are reached after 24hours (‘35’ patches) or 12hours (‘70’ patches) hence alternative analgesia must be available during this time.
- Alternative or ‘breakthrough’ analgesia can be achieved with buprenorphine sublingual tablets (maximum 0.2mg x 3 in 24hours) or by 4 hourly morphine equivalent.
- Constipation may be less likely to occur therefore routine laxatives may not be required.
- Maximum recommended dose = 2 x ‘70’ patches equivalent to 240mg oral morphine per 24hours.

N.B Unlike most opioid analgesics buprenorphine’s effects are only **partially reversed** by naloxone.

IF IN DOUBT SEEK SPECIALIST ADVICE

FENTANYL

Fentanyl is a synthetic opioid - like morphine it is a mu-agonist and potent analgesic. Fentanyl is on the top (third) step of the WHO Analgesic Ladder (see Factsheet 6). Fentanyl patches give slow, prolonged transdermal release, hence therapeutic levels are attained slowly

Dose Selection

‘25’ FENTANYL patch/72hrs \cong 90mg. oral MORPHINE /24hrs

The strength of the initial fentanyl patch should be based on the patient's previous 24-hour opioid requirement, and the general condition of the patient (see precautions page 1 and side-effects page 6). Patients who have only received weak opioids should commence on 12 microgram per hour patch.

NB It is strongly advised that specialist advice is sought if fentanyl requirements appear to exceed 200 micrograms per hour.

Conversion from oral morphine/Subcutaneous diamorphine to fentanyl patch		
Total 24hour oral morphine mg dose	Fentanyl micrograms per hour	Total 24hour subcutaneous diamorphine mg
30 to 59	12	10 to 19
60 to 134	25	20 to 44
135 to 224	50	45 to 74
225 to 314	75	75 to 104
315 to 404	100	105 to 134
405 to 494	125	135 to 164
495 to 594	150	165 to 194
595 to 674	175	195 to 224
675 to 764	200	225 to 255

Conversion to fentanyl patch

- There is no direct conversion between fentanyl dose and morphine dose, therefore always consult tables (and use clinical judgement).
- After application of patch, therapeutic levels are achieved slowly, breakthrough (prn) medication may be required during this time. Therapeutic levels are reached and maintained between 24 and 72 hours. Therefore after application assess efficacy of patch after 48-72 hours, if breakthrough doses are required regularly, it may be an indication to either increase the strength of the fentanyl patch or convert to other opioid formulation.
- Each patch lasts 72 hours, and should be replaced after this time. (Therapeutic levels continue).
- From short acting (4 hourly) oral morphine sulphate:
apply patch - monitor patient 4 hourly for analgesic requirement - expect to continue 4 hourly doses for first 12 to 24 hours.
- From 12 hourly morphine:
apply the first patch at the same time as taking the final 12 hourly tablet. Continue breakthrough 'prn' medication as required.
- From syringe driver:
apply patch - monitor patient at least 4 hourly for signs of toxicity, then remove syringe driver once patch in place for 12 hours.

Note: Different formulations (matrix and reservoir) of fentanyl are available. Different fentanyl products are **not** interchangeable, prescribe by brand name.

ALWAYS prescribe “breakthrough” (as required - prn) doses of either oral morphine or subcutaneous diamorphine for patients on fentanyl, to meet any change in analgesic requirement.

“Breakthrough” doses

Fentanyl patch strength (micrograms per hour)	Oral short acting morphine dose mg 4 hourly	Subcutaneous diamorphine dose mg 4 hourly
12	10	2.5 to 5
25	20	5 to 10
50	25 to 35	10 to 15
75	40 to 50	15 to 20
100	55 to 65	20
125	70 to 80	20 to 25
150	85 to 95	25 to 30
175	100 to 110	30 to 35

Conversion from fentanyl to oral morphine/subcutaneous diamorphine

NB. When converting from fentanyl to either oral morphine or subcutaneous diamorphine the conversion is not direct, and varies from patient to patient. Consult tables and use a dose from the lower end of the predicted range, titrating as necessary until correct dose established.

Conversion from fentanyl may become necessary when analgesic requirements are changing, due to change in patient’s disease or improvement/deterioration in patient’s general condition. In the terminal phase of disease, opioid requirements may increase due to accelerating disease, or decrease due to diminishing renal and/or hepatic function.

After removal of patch

- Fentanyl remaining in the skin will continue to enter the circulation providing analgesia for a variable period up to 17 hours.
- Orally use “breakthrough” dose morphine (see table) as necessary for 12 hours, then regular 4 hourly morphine titrating until pain control achieved.
- Subcutaneously use “breakthrough” diamorphine (see table) as necessary during first 12 hours THEN COMMENCE subcutaneous diamorphine pump.
- Where titrated dose of oral morphine equal to or less than 10mg consider substituting with weak opioid e.g. codeine.
- To dispose of used patch - fold patch in half adhesive sides together, place in clinical waste (hospital) or household waste (community).

SIDE-EFFECTS OF TRANSDERMAL OPIOIDS

Are similar to those of other strong opioid mu-agonists (e.g. morphine)

- nausea and vomiting
- drowsiness
- constipation
- dizziness
- confusion and hallucinations
- sweating

Opioids reduce gut motility causing:

- nausea** this may be negligible in some patients, others require antiemetic (e.g. metoclopramide 10mg tds) during the first few days of treatment and whenever opioid dose is increased.
- constipation** a laxative combining softening and propellant/stimulant activity should be prescribed. See Factsheet 12.

Side-effects experienced when an opioid is commenced or increased often diminish over the subsequent 48 to 72 hours. Sudden cessation of opioid treatment will cause opioid withdrawal syndrome.

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General palliative care references include:

'Palliative Care Formulary', Fourth Edition (PCF4) Edits: Robert Twycross and Andrew Wilcock available via Palliativedrugs.com

Palliative Adult Network Guidelines Third Edition (also available as an App)
Edits: Max Watson, Caroline Lucas, Andrew Hoy, Ian Back, Peter Armstrong

Take note of:

NICE (National Institute for Health and Clinical Excellence) clinical guideline 140:
Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults

NPSA Rapid Response Report NBA/2008/RRR05 "Reducing Dosing Errors with Opioid Medicines":