

Fentanyl patches

FENTANYL IS A SYNTHETIC OPIOID which is available as a transdermal patch. This allows controlled delivery of the drug for up to 72 hours. Transdermal fentanyl is potentially useful if the patient has experienced intolerable adverse effects to morphine or is unable to take oral analgesia. The fentanyl patch is a less flexible dose form than oral morphine and is best reserved for patients with stable opioid requirements.

PHARMAC is to widen access to subsidised fentanyl patches in 2009, via listing a new brand of patches without the requirement for Special Authority (subject to Medsafe registration of the new brand of patch). This will mean that GPs will be able to prescribe funded fentanyl patches for their patients. Fentanyl will be available as 25, 50, 75 and 100mcg/hour transdermal patches.

As GPs may be unfamiliar with using fentanyl patches the following information is provided to ensure patient safety.

Who are fentanyl patches suitable for?

Fentanyl patches are best reserved for people with chronic pain and stable opioid requirements who are unable to take morphine orally.^{1,2}

They may also be suitable for people who have intolerable side effects to morphine (e.g. intractable constipation) or who are in renal failure.

Who are fentanyl patches not suitable for?

Fentanyl patches are not suitable for opioid naïve patients with non-cancer pain.^{1,2} These patients are vulnerable to potentially fatal opioid effects such as respiratory depression.

Fentanyl patches should not be used for rapid titration in pain control. Fentanyl patches have a 6–17 hour half life and take at least 24 hours to reach a steady plasma level. If a patient is suffering from serious adverse effects e.g. respiratory depression, on removal of the patch it will take at least 24 hours for levels to drop significantly.

Cautions when using fentanyl patches

- Prescribe with care to elderly and debilitated patients – the elimination half-life may be prolonged. Elderly patients may also have increased sensitivity to the effects of fentanyl. Reduced doses should be used in elderly or debilitated people and they should be observed carefully for signs of toxicity and the dose reduced if necessary.³
- Fentanyl patches cannot be cut in half, therefore there is no recommended way to modify the doses available.
- Increased blood flow to the skin will increase blood fentanyl levels. Avoid placing localised sources of heat such as hot-water bottles directly over the patch. Care needs to be taken with electric blankets. To avoid problems with hot baths the patches should be placed on the upper body only. Showers do not usually cause a problem but in all cases extra care is needed with vulnerable patients such as elderly people.

- Potential interactions. Concomitant use of CYP3A4 inhibitors such as itraconazole or erythromycin may lead to potentially dangerous increases in fentanyl levels. Adverse effects of fentanyl may be potentiated by other CNS depressants.
- Patches can lose adherence in which case they can be covered by a waterproof dressing.
- Fentanyl patches need to be disposed of carefully because a significant amount of fentanyl is left in the patch after three days. Discarded patches have the potential to be misused.

Dosing for fentanyl patches

The initial dose of fentanyl should be the lowest possible dose based on the patient's opioid history and current medical status. The dose can be titrated upwards as required.

Ideally patients are initially titrated with other opioids and then converted to fentanyl patches. For some cancer pain, it may be suitable to initiate treatment with a fentanyl patch. In this case, start with the lowest strength patch and titrate upwards. It can take 24–48 hours to reach an effective plasma concentration so previous medication should be phased out gradually.

The dose of the initial fentanyl patch is based on the morphine equivalent daily dose currently used by the patient.

1. Assess current 24-hour opioid use.
2. If not using morphine, convert this to a 24 hour oral morphine equivalent dose.
3. Based on this estimated 24-hour equivalent oral morphine dose, work out the recommended fentanyl patch dose.

Two examples are:

Patient on stable dose of morphine

E.g. Stable daily morphine dose is 90mg. Referring to the manufacturers data (Table 1) shows that the recommended

fentanyl dose for this level of morphine is 25mcg per hour. The 25mcg fentanyl patch should be applied with the final dose of long-acting morphine. As with all opioid use, remember the rules of “ABC”:

- A** consider prescribing an **antiemetic** for nausea
- B** calculate a **breakthrough** dose based on one sixth of the morphine equivalent daily dose. In this example, this would be 10–15mg taken as required.
- C Constipation.** Fentanyl may be less constipating in individual patients, consider reducing laxative dose.

Patient on stable dose of other opioid

E.g. stable daily oxycodone dose is 160mg. Referring to the conversion (Table 2) shows that this is equivalent to 240-320mg morphine/day. Table 1 shows that the recommended fentanyl dose is either 75 or 100 mcg per hour. Consider using the lowest dose fentanyl patch recommended and then increasing if required.

Again, remember ABC. The breakthrough dose is 40 to 50 mg morphine or oxycodone equivalent.

Review the patient the following day. If they are very drowsy and opioid overdose is suspected remove the patch immediately and consider admission to hospital. If the dose is tolerated, but pain is not controlled, encourage use of breakthrough medication and review over the next two days. Continue to monitor gastrointestinal effects. Once a stable state is reached it is possible to titrate with the fentanyl patch. Remember to increase the breakthrough dose.

Very rarely patients metabolise fentanyl more quickly than normal and develop pain on day three. If this is a regular pattern, it is reasonable to swap from 72 hour dosing to 48 hour dosing.

Table 1: Recommended fentanyl dose based on daily oral morphine dose

Oral 24-hour morphine (mg/day)	Fentanyl dose (micrograms/hour)
60 -134	25
135 - 224	50
225 - 314	75
315 -404	100
405 - 494	125
495 - 584	150
585 - 674	175
675 - 764	200
765 - 854	225
855 - 944	250
945 - 1034	275
1035 - 1124	300

Table 2: Morphine equivalent doses⁴.

	Equivalent to 10mg morphine (oral)	Ratio
Codeine	100mg	0.1
Dihydrocodeine	100mg	0.1
Tramadol	50mg	0.2
Oxycodone (oral)	5 - 7.5 mg	1.5 - 2
Methadone (oral)	Varies depending on length and dose of opioid use. Specialist advice is needed.	5 - 20

N.B. The dose conversion tables provided by manufacturers are intended as a guide and individual patients may vary in their response to fentanyl. Consider using a lower-dose patch initially and titrating upwards.

Prescribers should inform patients about the correct use of fentanyl patches:

Stopping fentanyl patches

Levels of fentanyl fall slowly after removal of the patch. Observe patients for adverse effects for up to 24 hours after removal of the patch. Withdrawal symptoms can still occur, if possible taper the dose to minimise these.¹

- Follow prescribed dose
- Apply the patches at the correct frequency
- Apply to non-hairy skin (but do not shave the area)
- Ensure old patches are removed when the new patch is applied
- Do not cut patches
- Store patches and dispose of used and unused patches safely

Prescribers should also educate patients and carers about the signs and symptoms of fentanyl overdose such as trouble breathing, extreme sleepiness, inability to walk, talk or think properly.

References:

1. NPS RADAR. Fentanyl patches (Durogesic) for chronic pain. Available from: http://www.nps.org.au/health_professionals/publications/nps_radar (Accessed August 2008).

Opioid titration

In some cases it is considered appropriate to initiate fentanyl patches in opioid-naïve patients, i.e. such as with cancer pain. It is recommended that these patients be first titrated with low doses of opioids until an equianalgesic dose equivalent to a 25 mcg/hour fentanyl patch is achieved.

Treatment is usually initiated with a short-acting immediate release opioid given every four to six hours. Usual starting doses are:

- Morphine 5 – 10 mg
- Oxycodone 5 mg

The patient can then be converted to a 25 mcg/hour fentanyl patch.²

2. Medsafe. Durogesic datasheet. Available from: www.medsafe.govt.nz. (Accessed August 2008).
3. Sweetman SC (ed), Martindale: The Complete Drug Reference 35. [online] London: Pharmaceutical Press. Available from: <http://www.medicinescomplete.com> (Accessed August 2008).
4. NHS. The use of strong opioids in palliative care. MeRec Briefing 2003; 22.