Properties and use of transdermal fentanyl

Steve Chaplin BPharm, MSc and Austin Leach FRCA, FFPMRCA

Steve Chaplin and Dr Austin Leach provide an overview of the properties of transdermal fentanyl preparations in the management of severe chronic pain in adults and opioid-tolerant children.

Steve Chaplin

Fentanyl is a strong opioid with a rapid onset and a short duration of action. It is available in several formulations, including buccal tablets and a film, a ‘lollipop’, an infusion and a nasal spray but it is most frequently prescribed in primary care as a transdermal patch, accounting for about one million prescriptions in England in 2012/13.

Choice

The patch is licensed for the long-term treatment of chronic severe pain in adults and in opioid-tolerant children over two years old. There are currently at least eight brands. They are available in similar but not identical ranges of strengths, releasing 12–100µg per hour for 72 hours (with the exception of Mezolar, the only brand with a patch delivering 37.5µg per hour).

Their basic NHS price varies according to brand, ranging from £7.52–£25.89 for 12µg formulation to £34.59–£86.46 for 100µg formulation. All except Fentails, which is a reservoir patch, are formulated as a matrix patch; there is probably little difference in efficacy but patients may prefer a matrix patch.¹

The summary of product characteristics (SPC) for Durogesic DTrans cautions that additional counselling is needed if the brand of patch is changed because release characteristics may differ between products but this is not repeated by other manufacturers.

Dose

Fentanyl patches are usually prescribed for patients switching from another opioid. The strength of patch is therefore determined by their previous opioid dose (equivalent doses are given in the SPC of each product). Adults who have not previously been taking an opioid should have an immediate-release formulation of morphine titrated against their pain to provide a basis for estimating the dose of transdermal fentanyl.

Dosage during use of a patch can be adjusted in increments of 12–25µg per hour but the patches should not be cut. High doses can be achieved by using more than one patch at a time but a requirement for doses in excess of 300µg per hour suggest the need for an additional or alternative method of administration. Additional analgesia for breakthrough pain may be needed.

Patients should be monitored for adverse effects during the first few days of using a patch. Effectiveness should not be
assessed until after 24 hours of changing the dose because blood levels plateau between 12 and 24 hours. Elderly people and patients with renal or hepatic impairment may need a reduced dose and should be more closely observed for adverse effects.

**Application**

Patches should be worn continuously, applying a new one after removal of the used one. The hands should be washed before and after application. The patch should be inspected and if damaged they should be returned to the pharmacy unused. It should be applied to dry healthy skin (ie not irritated or irradiated), usually on the torso or upper arm in adults or, in children, on the back to prevent them fiddling with it. The application area should not be hairy (or clipped if it is, not shaved) and it should be cleaned with water – soap, lotions and other cleaners may impair adhesion. The site of application should be rotated.

Heat applied to the patch – including such diverse sources as an electric blanket, a hot bath or sunbathing – increases the rate of absorption of fentanyl sufficient to cause adverse effects. The patch should therefore be protected from strong sunlight when worn. A fever of 40°C may be enough to raise blood levels by 30 per cent.

**Removal**

Blood levels of fentanyl decline relatively slowly after a patch has been removed. This is due to continued absorption from the skin depot, resulting in an effective elimination half-life of 13–22 hours in adults and 22–25 hours in children. The slow decline means that substitution of an alternative opioid should be gradual, beginning with a low dose. This lingering action is also important to consider when the patch has been removed in response to adverse effects.

**Writing prescriptions**

The fentanyl patch is a Class 2 Controlled Drug. The prescription should state the strength (as the release rate – ie fentanyl 50 patch) and the interval between applying patches (ie one patch every 72 hours). The total quantity of patches to be supplied should be written in words and figures.

**Drug interactions**

Fentanyl undergoes extensive hepatic conversion to an inactive metabolite. It should not be co-prescribed with a strong inhibitor of CYP3A4 (eg clarithromycin, verapamil, diltiazem, some antifungal agents and some protease inhibitors). Concurrent use of saquinavir (Invirase) may be associated with an increased risk of ventricular arrhythmias.

Dose adjustment may be needed if fentanyl is co-prescribed with a strong enzyme inducer such as rifampicin, carbamazepine or phenytoin. As with other opioids, there is a risk of serotoninergic effects if fentanyl is used together with an MAOI or SSRI antidepressant.

**Advice to patients and carers**

Health professionals should ensure patients and carers have a product information leaflet and go through it with them. They should be counselled about the adverse effects of opioids and advised to follow dose instructions carefully. A patch should be removed immediately if breathing difficulty, marked drowsiness, confusion, dizziness or impaired speech occur, and patients and carers should seek prompt medical attention.

Patients should also be warned that treatment may cause drowsiness and impair psychomotor coordination sufficient to affect driving or use of machinery. Patients should be advised they would be committing an offence if they drive while adversely affected by fentanyl (but not if they are unaffected).

It is important to dispose of used patches safely because they contain significant amounts of fentanyl. They should be folded in half to prevent inadvertent contact with the inner surface and returned to the pharmacy.

**Declaration of interests**

Steve Chaplin has none to declare.

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**Place in therapy**

**Austin Leach**

The role of strong opioid painkilling drugs in the management of pain associated with cancer has been well established for many years. In recent years it has become accepted that strong opioids are also appropriate therapy for long-term pain not related to malignancy. There is a substantial evidence base that supports their use and which refutes many of the myths that remain stubbornly widespread within many healthcare professional disciplines.

Fear of addiction and the development of drug misuse behaviour are commonplace among patients; some prescribers share these concerns. However, it is important not to confl ate the development of drug tolerance (which may be associated with withdrawal symptoms if the drug is suddenly stopped) with drug addiction, which describes a behavioural disorder that focuses on acquisition of the drug by any means (‘drug-seeking behaviour’). The likelihood of a patient without risk factors becoming addicted to prescribed opioids is less than 1 per cent.

Fentanyl is usually prescribed to patients who find their pain is opioid-sensitive, but other strong opioids (such as modified-release morphine or oxycodone) cause well-recognised but unacceptable side-effects. Fentanyl is also the step 3 opioid of choice in patients with unreliable oral intake.

If renal function is poor, fentanyl is a more predictable opioid than morphine since it is less dependent on the kidney for excretion. Some patients have a preference for transdermal administration and to ensure good adherence such a preparation may be the first choice. Long-term use may suppress the hypothalamic-pituitary axis and reduced testosterone production has been reported.
A study in patients with malignancy-associated pain showed a reduced incidence of constipation and daytime drowsiness with transdermal fentanyl in comparison to oral modified-release morphine. Because of the ‘depot effect’ caused by the subdermal reservoir, dosage adjustment may take days to achieve satisfactorily and rapidly-acting breakthrough supplements may be used more frequently during upward titrations, which should be closely supervised.

There are several fentanyl preparations for breakthrough pain management (lozenges, ‘lollipops’, metered nasal spray), which are members of a group of agents known as ‘rapid-onset opioids’ (ROOs). These drugs have a short-term therapeutic effect. However, in many circumstances rapid onset and offset may not be appropriate or desirable. The usual way of managing breakthrough pain is to prescribe an opioid with a longer action than the ROOs; it is appropriate to use normal-release step 3 opioids (e.g. morphine) unless oral drugs are to be avoided. The longer action of preparations such as morphine elixir may actually provide more effective breakthrough relief, despite the ‘technical difficulty’ of mixing strong opioids.

There is plenty of readily available advice and support. NICE has published guidelines (CG140) on the use of opioids in palliative care and the British Pain Society has published separate guidance for health professionals and patients (Opioids for Persistent Pain: Good Practice and Opioids for Persistent Pain: Information for Patients), which are available from the British Pain Society website (www.britishpainsociety.org).

Declaration of interests
Dr Leach has none to declare.

Dr Leach is a consultant in pain medicine and anaesthesia at the Royal Liverpool and Broadgreen University Hospitals NHS Trust.