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To All GPs and Pharmacists

Please Retain for Future Reference

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Prescribing of Fentanyl (Matrifen) Patches

Dear Colleague

Adverse Incident

Recently there has been a serious incident locally when a patient has suffered respiratory arrest precipitated by Fentanyl overdose; the patient was initiated on Fentanyl Patches and was relatively opiate-naive. Following on from this incident the Medicines Management Team felt it was important to provide some information to support prescribers and pharmacists when they are considering prescribing and dispensing of this potent opiate analgesic in patch form.

Therapeutic Indication

The below information considers the prescribing of Fentanyl Patches for adults for the therapeutic indications of

- in the management of chronic intractable pain due to cancer
- in the management of chronic intractable pain.

Fentanyl Patches are also indicated for use in children, for the long term management of severe chronic pain in children receiving opioid therapy from 2 years of age but prescribing for this indication is not covered in the below information. Any prescriber requiring support or advice in prescribing Fentanyl for a child can contact the Medicines Management Team directly.

Method of Administration

Fentanyl Patches are transdermal patches that should be applied to non-irritated and non-irradiated skin on a flat surface of the torso or upper arm. A non-hairy area should be selected. If this is not possible, hair at the application site should be clipped (not shaved) prior to application. If the site of Fentanyl Patch application requires to be cleansed prior to application of the patch, this should be done with water. Soaps, oils, lotions or any other agent that might irritate the skin or alter its characteristics should not be used. The skin should be completely dry before the patch is applied. Patches should be inspected prior to use. Patches that are cut, divided, or damaged in any way should not be used.

Fentanyl Patch should be applied immediately after removal from the sealed pouch. Avoid touching the adhesive side of the patch. Following removal of both parts of the protective liner, the transdermal patch should be pressed firmly in place with the palm of the hand for approximately 30 seconds, making sure the contact is complete, especially around the edges. Then wash hands with clean water.

Fentanyl Patch should be worn continuously for 72 hours. A new patch should then be applied to a different skin site after removal of the previous transdermal patch. Several days should elapse before a new patch is applied to the same area of skin. The need for continued treatment should be assessed at regular intervals.

Dose Selection

Initial dose selection

The appropriate initiating dose of Fentanyl Patch should be based on the patient's current opioid use. It is recommended that Fentanyl Patch be used in patients who have demonstrated opioid tolerance. Other factors to be considered are the current general condition and medical status of the patient, including body size, age, and extent of debilitation as well as degree of opioid tolerance.

Opioid-tolerant patients

To convert opioid-tolerant patients from oral or parenteral opioids to Fentanyl Patch refer to *Equianalgesic potency conversion* below. The dosage may subsequently be titrated upwards or downwards, if required, in increments of either 12 or 25 mcg/hr to achieve the lowest appropriate dose of Fentanyl Patch depending on response and supplementary analgesic requirements.

Opioid-naive patients

In the Drug Safety Update issued by MHRA in September 2008 it advised that Fentanyl patches should be used only in patients who have previously tolerated opioids because of a risk of significant respiratory depression in opioid-naïve patients

Equianalgesic potency conversion

1. Calculate the previous 24-hour analgesic requirement.
2. Convert this amount to the equianalgesic oral morphine dose using Table 1.
3. To derive the dosage of Fentanyl Patch corresponding to the calculated 24-hour, equianalgesic morphine dosage, use the dosage-conversion Table 2 or Table 3.

Table 1: Equianalgesic Doses All IM and oral doses in this chart are considered equivalent to 10 mg of IM morphine in analgesic effect.

Drug name	***Equianalgesic dose (mg)***	
	IM*	***oral***
morphine	*10*	*30-40 (assuming repeated dosing)***
hydromorphone	*1.5*	*7.5*
methadone	*10*	*20*
oxycodone	*15*	*30*
levorphanol	*2*	*4*
oxymorphone	*1*	*10 (rectal)*
diamorphine	*5*	*60*
pethidine	*75*	*—*
codeine	*130*	*200*
buprenorphine	*0.4*	*0.8 (sublingual)*

** Based on single-dose studies in which an IM dose of each drug listed was compared with morphine to establish the relative potency. Oral doses are those recommended when changing from a parenteral to an oral route. ** The oral/IM potency for morphine is based on clinical experience in patients with chronic pain.* Reference: Adapted from Foley KM. The treatment of cancer pain. NEJM 1985; 313 (2): 84-95, with updates.

Table 2 is for adult patients who have been stabilised on oral morphine or another immediate-release opioid only over several weeks i.e. relatively opiate-naive (conversion ratio of oral morphine to transdermal Fentanyl approximately equal to 150:1). This is a more cautious regimen.

Oral 24-hour morphine (mg/day)	***Fentanyl Patch Dosage (mcg/hr)***
<135	*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*

[1] *In clinical trials these ranges of daily oral morphine dosages were used as a basis for conversion to Fentanyl Patch.*

Table 3 is for highly opioid-tolerant adult patients who have been on a stable and well-tolerated opioid regimen for a long period (conversion ratio of oral morphine to transdermal Fentanyl approximately equal to 100:1). This regimen concurs with equivalence table found in the BNF 63 March 2012 p21.

Oral 24-hour morphine (mg/day)	***Fentanyl Patch Dosage (mcg/hr)***
< 44	*12*
45-89	*25*
90-149	*50*
150-209	*75*
210-269	*100*
270-329	*125*
330-389	*150*
390-449	*175*
450-509	*200*
510-569	*225*
570-629	*250*
630-689	*275*
690-749	*300*

Tables 2 and 3 should not be used to switch from transdermal Fentanyl to another opioid treatment.

Previous analgesic therapy should be phased out gradually from the time of the first patch application until analgesic efficacy with Fentanyl Patch is attained. For both strong opioid-naïve and opioid tolerant patients, the initial evaluation of the analgesic effect of Fentanyl Patch should not be made until the patch has been worn for 24 hours due to the gradual increase in serum Fentanyl concentrations up to this time.

Dose titration and maintenance therapy

The Fentanyl Patch should be replaced every 72 hours. The dose should be titrated individually until a balance between analgesic efficacy and tolerability is attained. In patients who experience a marked decrease in the period 48-72 hours after application, replacement of Fentanyl Patch after 48 hours may be necessary. If analgesia is insufficient at the end of the initial application period, the dose may be increased.

Dose adjustment, when necessary, should normally be performed in the following titration steps from 25 mcg/hr up to 75 mcg/hr: 25 mcg/hr, 37 mcg/hr, 50 mcg/hr, 62 mcg/hr and 75 mcg/hr; thereafter dose adjustments should normally be performed in 25 mcg/hr increments, although the supplementary analgesic requirements (oral morphine 90 mg/day ≈ Fentanyl Patch 25 mcg/hr) and pain status of the patient should be taken into account.

More than one Fentanyl Patch may be used to achieve the desired dose.

Patients may require periodic supplemental doses of a short-acting analgesic for 'breakthrough' pain. Additional or alternative methods of analgesia should be considered when the Fentanyl Patch dose exceeds 300 mcg/hr.

Increased body temperature, exposure of patches to external heat sources, and concomitant use of CYP3A4 inhibitors may lead to potentially dangerous rises in serum Fentanyl levels. Concomitant use of other CNS depressants might also potentiate adverse effects from Fentanyl.

Advice to Patients and Carers

Healthcare professionals, particularly those who prescribe and dispense Fentanyl patches, must fully inform patients and caregivers about directions for safe use:

- follow the prescribed dose
- follow the correct frequency of patch application
- ensure that old patches are removed before applying a new one
- patches must not be cut
- avoid touching the adhesive side of patches and wash hands after application
- follow instructions for safe storage and disposal of used or un-needed patches.

Healthcare professionals, particularly those who prescribe and dispense Fentanyl patches, should ensure that patients and caregivers are aware of the signs and symptoms of Fentanyl overdose, namely:

- trouble breathing or shallow breathing
- tiredness; extreme sleepiness or sedation
- inability to think, walk, or talk normally; and feeling faint, dizzy, or confused.

Patients and caregivers should be advised to seek medical attention immediately if overdose is suspected

Patients who experience serious adverse events should have the patches removed immediately and be monitored

Discontinuation of Fentanyl Patch

If discontinuation of Fentanyl Patch is necessary, any replacement with other opioids should be gradual, starting at a low dose and increasing slowly. This is because Fentanyl concentrations fall gradually after Fentanyl Patch is removed; the half-life of Fentanyl is 17 hours or more.

Use in elderly patients

Data from intravenous studies with Fentanyl suggest that elderly patients may have reduced clearance, a prolonged half-life and they may be more sensitive to the drug than younger patients. Elderly, cachectic, or debilitated patients should be observed carefully for signs of Fentanyl toxicity and the dose reduced if necessary.

We hope you find this information helpful. If you have any further questions or require any further support please don't hesitate to contact the Medicines Management Team.

Regards

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