MHRA Safety Alert published 11th October 2018

Transdermal fentanyl patches: life-threatening and fatal opioid toxicity from accidental exposure, particularly in children

Detailed below are the salient points of the MHRA alert; it is recommended that prescribers take this opportunity to review their prescribing of fentanyl patches to determine whether they continue to be appropriate – see Appendix A for information.

Background

Accidental exposure to transdermal fentanyl can occur if a patch is swallowed or transferred to another individual, (see Drug Safety Update, September 2008, and Drug Safety Update, July 2014).

In 2014, following an EU review, advice on minimising risk of accidental transfer was added to Summary of Product Characteristics and the Patient Information Leaflet for transdermal fentanyl products.

In December 2015, Welsh Government issued a Patient Safety Notice regarding the risk of harm from the inappropriate use and disposal of fentanyl patches.

Since July 2014 and up to October 2018, the MHRA have received 5 reports of fatal incidents specifying accidental exposure, accidental overdose, or product adhesion issue. Causes of death was not included in all reports but were understood to be related to opioid toxicity.

Children are at risk as they may touch, suck, chew, or swallow a patch that has not been disposed of properly; also, children have a lower threshold for fentanyl overdose than adults do.

All healthcare professionals, particularly those involved in the prescribing and dispensing of fentanyl patches, should provide clear information to patients and caregivers regarding risk of accidental transfer and ingestion of patches, and the need for appropriate disposal of patches.

Advise patients and caregivers to follow the instructions on the patch packaging, the carton and in the accompanying patient information leaflet. To help you discuss this with patients, the MHRA have produced an updated patient and caregiver information sheet (large print version).

An additional counselling resource titled Safeguarding Users of Opioid Patches by Standardising Patient/Caregiver Counselling is also available from AWMSG.
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The MHRA has issued the following advice for healthcare professionals:

- always fully inform patients and their caregivers about directions for safe use for fentanyl patches, including the importance of:
  - not exceeding the prescribed dose
  - following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application
  - not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower)
  - ensuring that old patches are removed before applying a new one
  - following instructions for safe storage and properly disposing of used patches or those which are not needed (see instructions below)

- ensure that patients and caregivers are aware of the signs and symptoms of fentanyl overdose (see below) and advise them to seek medical attention immediately (by dialing 999 and requesting an ambulance) if overdose is suspected

- in patients who experience serious adverse events, remove patches immediately and monitor for up to 24 hours after patch removal

- if a patch is transferred to another person, it should be removed and the individual should get medical help immediately

- if a patch is swallowed, the individual should get medical help immediately

- report any cases of accidental exposure where harm has occurred or suspected side effects via the Yellow Card Scheme
Appendix A
Prescribing review information—Transdermal fentanyl patches

1. NICE CG140\(^1\) states the first-line choice strong opioid is sustained release (SR) oral morphine, with immediate release oral morphine for breakthrough pain.

Consider reserving opioid patches for pain only for the following:

- **Patients unable to tolerate tablets due to side effects, or have difficulty swallowing (although oral liquids and subcutaneous morphine may be suitable alternatives instead of a patch)**\(^2\)

- **Patients with compliance issues such as mental health problems, or who are socially isolated with limited access to care**\(^2\)

Basis for the recommendation

- Transdermal formulations lack the flexibility required when treating patients with fluctuating or uncontrolled pain

- The relative potency of formulations is not fully appreciated by some prescribers

- There have been a number of safety incidents associated with accidental transfer or exposure of patches to another person and increased absorption of medication from patches on exposure to heat and after failure to remove old patches

- Inappropriate use of transdermal formulations has cost implications, as fentanyl is several times more costly than equivalent doses of oral analgesics

- It is recognised that some patients cannot take or tolerate oral medications; in this instance, patients should have access to alternative formulations of pain relief
Appendix A
Prescribing review information—Transdermal fentanyl patches
Continued

2. NICE KTT21\(^3\) includes reference to the opioids aware resource\(^4\), which provides a helpful summary of the evidence considering the effectiveness of opioids for long-term pain\(^5\). It concludes that:

- There is little evidence that opioids are helpful for long-term (chronic) pain.
- A small proportion of people may obtain good pain relief with opioids in the long term if the dose can be kept low and use is intermittent, but it is difficult to identify these people at the start of treatment.
- The risk of harm increases substantially at doses above an oral morphine equivalent of 120 mg/day, but there is no increased benefit.
- Opioids should be discontinued if the person is still in pain despite using opioids, even if no other treatment is available.
- A detailed assessment of the emotional influences on the person's pain experience is essential for people with long-term (chronic) pain who also have refractory and disabling symptoms, particularly if they are on high opioid doses.

The opioids aware resource\(^4\) also contains key points on the clinical use of opioids for long-term (chronic) pain. It highlights that people with chronic pain who do not achieve useful pain relief from opioids within 2 to 4 weeks are unlikely to gain benefit in the long term, and that people who may benefit from opioids in the long term will demonstrate a favourable response within 2 to 4 weeks.

3. NICE’s medicines evidence commentary on chronic pain: patient outcomes with dose reduction or discontinuation of long-term opioid therapy\(^6\) discusses a systematic review which found that there was some evidence that several types of intervention may be effective at reducing or discontinuing long-term opioid therapy and that pain, function and quality of life may actually improve with opioid dose reduction.

References
2. PrescQIPP Bulletin 80 Opioid patches – appropriate prescribing and use Accessed 16/10/18
4. Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. Faculty of Pain Medicine Accessed 16/10/18
5. The Effectiveness of Opioids for Long Term Pain. Faculty of Pain Medicine Accessed 16/10/18
6. NICE Medicines Evidence Commentary. Chronic pain: patient outcomes with dose reduction or discontinuation of long-term opioid therapy. Published November 2017