PRAC recommendation
Fentanyl patches – accidental exposure

This is a recommendation from the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA).

1. Administrative details

<table>
<thead>
<tr>
<th>Substance (invented name)</th>
<th>Fentanyl</th>
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<tbody>
<tr>
<td>Authorisation procedure</td>
<td>Non-centralised</td>
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<tr>
<td>Signal (EPITT No)</td>
<td>Accidental exposure (MedDRA PT) EPITT Ref. 17778</td>
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<tr>
<td>PRAC meeting date</td>
<td>07 – 10 April 2014</td>
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<tr>
<td>Signal identifier</td>
<td>Netherlands</td>
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<tr>
<td>PRAC rapporteur(s)</td>
<td>Sabine Straus (NL)</td>
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<tr>
<td>Name of product team leader</td>
<td>N/A</td>
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<td>Name of scientific administrator</td>
<td>Cosimo Zaccaria</td>
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<tr>
<td>Status</td>
<td>Signal follow-up</td>
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<td>Date of adoption</td>
<td>10 April 2014</td>
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2. Prioritisation and recommendation

Evidence evaluated and prioritisation/public health importance

In the fentanyl patches product information warnings and precautions for use regarding accidental exposure and instructions on the handling and disposal of used and unused patches are included.

It is therefore agreed with the MAH that this issue is not a new safety concern. However, cases of accidental exposure and medication error do occur and in some instances with a fatal outcome. The cumulative review of cases reporting accidental exposure/medication error with Fentanyl TTS Matrix
Patch or Patch, provided by the MAH, retrieved 1,557 cases in the EEA and 6,959 cases in non-EEA countries. While the majority (97.6%) of the reported events concerned non-serious events, serious cases, including 6 fatal cases (EEA and non-EEA), have been reported. Of these six fatal cases, all concerned children. The majority of the cases concerned adults, however in 3,000 cases age was not reported.

The lack of patch visibility may have contributed to the serious cases. It is therefore proposed to implement risk minimisation measures in line with those imposed in the US, i.e. improve patch visibility of all fentanyl TTS. The timelines should be ambitious to be proportionate to the seriousness of the risk of accidental exposure (especially in children) and medication error. The MAH should assess the effectiveness of these risk minimisation measures and based on the outcome of that evaluation, further measures might be warranted. Based on the current data the assessment of the spontaneous cases both qualitative (analysis of narratives) and quantitative (reporting rates) in the PSUR seems to be the best option to evaluate the risk minimisation measures.

The proposed DHPC by the MAH as a further risk minimisation measure to highlight and reinforce regarding accidental exposure and proper disposal of the patches is supported by the PRAC. The DHPC should provide information on how to minimise this risk. Patients (and caregivers) should be informed and instructed by their HCP (also when they are already using fentanyl TTS). The ultimate timing of circulation of the DHPC was discussed at the PRAC.

At this moment, it is agreed with the MAH that routine pharmacovigilance is considered sufficient to monitor accidental exposure and medication error reported with fentanyl TTS.

In the product information a warning (SmPC section 4.4) regarding accidental exposure and precautions for disposal (SmPC section 6.6) are included. MAH strengthened the warning on accidental exposure by patch transfer in May 2012. The MAH stated that there are still a few countries in the EU where the inclusion of the strengthened wording in the product information regarding accidental exposure is still pending.

**Recommendation**

Following the assessment of the cumulative review performed by the Marketing Authorisation Holder (MAH), the Pharmacovigilance Risk Assessment Committee (PRAC) recommended that Johnson and Johnson Pharmaceutical should submit to the National Competent Authority (NCA) within one month proposals on how to improve patch visibility and timelines for implementation.

The PRAC endorsed the MAH’s proposal to circulate a Direct Healthcare Professional Communication (DHPC) to highlight to Healthcare Professionals (HCPs) the risk of accidental exposure leading to fatal outcomes especially in children. The initial draft should be submitted to the PRAC within 2 weeks and should include measures to minimize the risk, provide clear instruction on how to inform the patient (including: always provide package leaflet) and reinforce the need for proper and safe disposal of the patches. In addition to the DHPC the PRAC also suggested educational material as an additional tool to further minimise the risk of accidental exposure to patients.

The PRAC agreed on the multifaceted nature of the risk and on the need to have a stepwise approach. The MAH should assess in the PSUR the effectiveness of the above risk minimisation measures evaluating spontaneous cases and the reporting rate. Based on the outcome of the evaluation, further measures might be warranted.

The PRAC recommended that Johnson and Johnson Pharmaceutical should submit within 1 month to the NCAs a variation or article 61.3 notification - as appropriate - to implement the strengthened wording in their Product Information (PI) as described below. The MAHs of generic products containing fentanyl TTS should update their PI in line with that of the reference product.
Summary of Product Characteristics (SmPC)

Section 4.4: Special warnings and precautions for use:

Accidental Exposure by Patch Transfer

Accidental transfer of a fentanyl patch to the skin of a non-patch wearer (particularly a child), while sharing a bed or being in close physical contact with a patch wearer, may result in an opioid overdose for the non-patch wearer. Patients should be advised that if accidental patch transfer occurs, the transferred patch must be removed immediately from the skin of the non-patch wearer. (see section 4.9 Overdose)

Use in Children

[...]

To guard against accidental ingestion by children, use caution when choosing the application site for [invented name] (see Section 6.6, Instructions for use/handling) and monitor adhesion of the patch closely."

Section 6.6: Instructions for use/handling

[...]

Used patches should be folded so that the adhesive side of the patch adheres to itself and then they should be safely discarded. Unused patches should be returned to the (hospital) pharmacy.

In line with the SmPC the wording in the PL should be, as follows

Package Leaflet (PL)

Section 2: Warning and precaution

[Product name] is a medicinal product that could be life threatening to children. This is also the case with used transdermal patches. Bear in mind that the design of this medicinal product could be tempting to a child which in some cases may lead to a fatal outcome. [Product name] can have life-threatening side effects in persons that are not using prescribed opioid medicines on a regular basis.

Patch sticking to another person

The patch should be used only on the skin of the person for whom it was ordered by the doctor. Cases have been reported where a patch was accidentally stuck to a family member while in close physical contact or sharing the same bed as the patch wearer. A patch sticking to another person (particularly a child) may result in an overdose. In case the patch sticks to the skin of another person, take the patch off immediately and seek medical attention.

Section 5: How to store

Keep unused and used [product name] patches out of children’s reach.

Handling the patch

Used patches should be folded so that the adhesive side of the patch adheres to itself and then they should be safely discarded. Accidental exposure to used and unused patches particularly in children may lead to a fatal outcome. Unused patches should be returned to the (hospital) pharmacy.