

## fentanyl

### Recommendations:

- **Amendments to the Product Information**

#### SmPC wording

General note: The following text should be included in the SmPC. If the Core Safety Profile as agreed upon during the previous PSUR Work Sharing procedure NL/H/PSUR/0030/001 already included a wording on the subject, the changes required as compared to the previous wording are indicated using underscores and ~~strike-through~~ text indicating text to be added and deleted, respectively.

- *For fentanyl transdermal patches*

#### **Section 4.4**

*Patients who have experienced serious adverse events should be monitored for ~~up to~~ at least 24 hours after Durogesic-~~<tradename>~~ removal, or more, as clinical symptoms dictate, ~~since~~ because serum fentanyl concentrations decline gradually and are reduced by about 50% 17 (range 13-22) hours later.*

#### **Section 4.4**

##### *Serotonin Syndrome*

*Caution is advised when <TRADENAME> is coadministered with drugs that affect the serotonergic neurotransmitter systems.*

*The development of a potentially life-threatening serotonin syndrome may occur with the concomitant use of serotonergic drugs such as Selective Serotonin Re-uptake Inhibitors (SSRIs) and Serotonin Norepinephrine Re-uptake Inhibitors (SNRIs), and with drugs which impair metabolism of serotonin (including Monoamine Oxidase Inhibitors [MAOIs]). This may occur within the recommended dose.*

*Serotonin syndrome may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea).*

*If serotonin syndrome is suspected, treatment with <TRADENAME> should be discontinued.*

#### **Section 4.4**

##### *Gastrointestinal Tract*

*Opioids increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. The resultant prolongation in gastrointestinal transit time may be responsible for the constipating effect of fentanyl. Patients should be advised to take measures to prevent constipation and prophylactic laxative use may be considered in some situations. Extra caution should be used in patients with*

*chronic constipation. If paralytic ileus is present or suspected, treatment with <TRADENAME> should be stopped.*

#### **Section 4.5**

##### *Serotonergic Drugs*

*Coadministration of fentanyl with a serotonergic agent, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) or a Monoamine Oxidase Inhibitor (MAOI), may increase the risk of serotonin syndrome, a potentially life-threatening condition.*

#### **Section 4.5**

*The concomitant use with CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin) could result in a decrease in fentanyl plasma concentrations and a decreased therapeutic effect. This may require a dose adjustment of transdermal fentanyl. After stopping the treatment of a CYP3A4 inducer, the effects of the inducer decline gradually and may result in a fentanyl plasma increase concentration which could increase or prolong both the therapeutic and adverse effects, and may cause serious respiratory depression. In this situation, careful monitoring and dose adjustment should be made if warranted.*

#### **For fentanyl solution for injection**

#### **Section 4.4**

*Caution is advised when <TRADENAME> is coadministered with drugs that affect the serotonergic neurotransmitter systems.*

*The development of a potentially life-threatening serotonin syndrome may occur with the concomitant use of serotonergic drugs such as Selective Serotonin Re-uptake Inhibitors (SSRIs) and Serotonin Norepinephrine Re-uptake Inhibitors (SNRIs), and with drugs which impair metabolism of serotonin (including Monoamine Oxidase Inhibitors [MAOIs]). This may occur within the recommended dose.*

*Serotonin syndrome may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea).*

*If serotonin syndrome is suspected, rapid discontinuation of <TRADENAME> should be considered.*

#### **Section 4.5**

##### *Serotonergic Drugs*

*Coadministration of fentanyl with a serotonergic agent, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) or a Monoamine Oxidase Inhibitor (MAOI), may increase the risk of serotonin syndrome, a potentially life-threatening condition.*

**Leaflet wording:**

The package leaflet should be updated in line with the recommendations for the SmPC, as appropriate.