

Effentora

Procedural steps taken and scientific information after the authorisation

No	Scope	Opinion/ Notification ¹ issued on	Commission Decision Issued ² / amended on	Product Information affected ³	Summary
II/0014	<p>Update of the Summary of Product Characteristics and Package Leaflet. Further to the availability of a revised Company Core Datasheet (CCDS) for Fentanyl Buccal Tablets, the MAH has updated the section 4.4 of the SmPC on the risk of respiratory depression with additional information concerning improper patient selection and/or improper dosing. The Package Leaflet has been updated accordingly.</p> <p>C.1.4 - Variations related to significant modifications of the Summary of Product Characteristics due in particular to new quality, pre-clinical, clinical or pharmacovigilance data</p>	20/10/2011	22/11/2011	SPC, PL	<p>Following the availability of a revised Company Core Datasheet (CCDS) the Product Information (section 4.4 of the SmPC and section 4 of the PL) for Effentora has been updated to reflect the fact that use of the product for conditions other than breakthrough pain in adults and/or improper dosing have resulted in clinically significant respiratory depression and fatalities. Editorial changes were made throughout the SmPC.</p> <p>Updated SmPC and PL are as follows:</p> <p>SmPC 4.4 Special Warnings and Precautions for Use Patients and their carers must be instructed that Effentora contains an active substance in an amount that can be fatal, especially to a child. Therefore they must keep all tablets out of the reach and sight of children. [...]</p> <p><u>Respiratory depression</u> As with all opioids, there is a risk of clinically significant respiratory depression associated with the use of fentanyl. Improper patient selection (e.g., use in patients without maintenance opioid therapy) and/or improper dosing have</p>

¹ Notifications are issued for type I variations (unless part of a group or a worksharing application). Opinions are issued for all other procedures.

² No Commission Decision is issued for type IA and type IB variations or for type II variations and annual re-assessments that do not affect the annexes.

³ SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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					<p>resulted in fatal outcome with Effentora as well as with other fentanyl products. Effentora should only be used for conditions specified in section 4.1.</p> <p>PL Section 4 (possible side effects) Effentora like other fentanyl products can cause very severe breathing problems which can lead to death.</p>
IA/0015/G	<p>This was an application for a group of variations.</p> <p>A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS,</p> <p>A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release),</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site,</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p>	23/05/2011	n/a		
IA/0013	B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place	08/12/2010	n/a		
IB/0011/G	<p>This was an application for a group of variations.</p> <p>Change of the EU/EEA Qualified Person for Pharmacovigilance (QPPV) and update of the Detailed Pharmacovigilance System (Version 1.3). Update of the organisation section of the Pharmacovigilance System in relation to the contact details of the QPPV and the name of the QPPV deputy. Update of other sections (Procedure, Database, Contractual Arrangements and Quality Management),</p>	26/08/2010	n/a	Annex II	<p>With this variation the MAH proposes to change the EU/EEA Qualified Person for Pharmacovigilance (QPPV) and to update the Detailed Pharmacovigilance System (Version 1.3). The organisation section of the Pharmacovigilance System in relation to the contact details of the QPPV, and the name of the QPPV deputy has been updated. Other sections (Procedure, Database, Contractual Arrangements and Quality Management), appendices and annex were also updated.</p>

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	<p>appendices and annex was also made.</p> <p>C.1.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV, C.1.9.z - Changes to an existing pharmacovigilance system as described in the DDPS - Other variation</p>				
IA/0012/G	<p>This was an application for a group of variations.</p> <p>A.7 - Administrative change - Deletion of manufacturing sites, B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing</p>	23/08/2010	n/a	Annex II, PL	
N/0010	<p>Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)</p>	05/07/2010	n/a	PL	
IB/0009	<p>42_a_01_Change in shelf-life of finished product - as packaged for sale</p>	25/01/2010	n/a	SPC	
II/0004	<p>Update of sections 4.2 and 5.2 of the Summary of Product Characteristics following a new bioequivalence study comparing the placement of the tablet within the mouth, between the cheek and the gum or sublingually and a publication. The Package Leaflet has been updated accordingly.</p> <p>Update of Summary of Product Characteristics and Package Leaflet</p>	24/09/2009	10/12/2009	SPC, PL	<p>The MAH submitted a publication and a bioequivalence study conducted to compare the pharmacokinetics of the buccal administration to the sublingual administration. The data supported sublingual tablet placement as an alternative to the currently approved buccal administration (above an upper rear molar between the cheek and gum). Consequently, section 4.2 of the SPC and section "Taking the medicine" of the PL were updated to reflect the possible sublingual placement of the tablet, and section 5.2 of the SPC was updated to include a reference to the results of the study proving bioequivalence between both sites for tablet placement within the buccal cavity.</p>
II/0005	<p>Update of section 5.3 of the SPC following completion of new carcinogenicity and developmental/reproductive studies.</p> <p>Update of Summary of Product Characteristics</p>	24/09/2009	10/12/2009	SPC	<p>The MAH submitted the results of new studies and section 5.3 was updated accordingly.</p> <p>A reference was included to a male-mediated effect in fertility and early embryonic development in rats at high doses.</p> <p>A reference was also included on the findings related to</p>

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					behavioural effects of fentanyl on pups, which may represent either a direct or an indirect effect on pups. Additionally the reference to the non-existence of carcinogenicity studies was deleted and the results of the carcinogenicity studies performed were included.
II/0003	Update to several sections of the SPC (4.2, 4.3, 4.4, 4.6, 4.8 and 4.9) for alignment with the CCDS. The Package Leaflet is updated accordingly. Also the phone numbers in the list of local representatives in the Package Leaflet have been updated. Finally, annex II is revised to include the conditions with regard to the safe and effective use of the medicinal product and to update the RMP version. Update of Summary of Product Characteristics and Package Leaflet	24/09/2009	10/12/2009	SPC, Annex II, PL	Sections 4.2 and 4.4 were revised to make the information clearer for the reader. In section 4.3, the use in acute pain other than breakthrough pain was added as a contraindication to strengthen the use in the approved indication. In section 4.6, a recommendation for breastfeeding not to be resumed within 48 hours of administration was included, reflecting the fact that fentanyl passes into breast milk. Events in section 4.8 revised to reflect post-marketing experience and clinical trial data. Several adverse events were added, others were reclassified in term of frequency and the event multiple myeloma was removed. A description of symptoms of overdose was added to section 4.9. Furthermore, annex II was revised to update the version of the latest approved RMP (version 1.4), and consequently to include reference to the educational materials included in the RMP.
IA/0008	07_a_Replacement/add. of manufacturing site: Secondary packaging site	16/09/2009	n/a		
IA/0007	07_a_Replacement/add. of manufacturing site: Secondary packaging site	07/09/2009	n/a		
II/0001	Update of the Detailed Description of the Pharmacovigilance System. Changes to QPPV, Update of DDPS (Pharmacovigilance)	23/04/2009	29/06/2009	Annex II	The Marketing Authorisation Holder applied to update the Detailed Description of the Pharmacovigilance System (DDPS) to change the Qualified Person for Pharmacovigilance. Consequently, annex II has been updated with identification of the version number of the DDPS as well as with the latest version number for the Risk Management Plan.
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/04/2009	n/a	PL	
IA/0002	08_a_Change in BR/QC testing - repl./add. of batch control/testing site	08/01/2009	n/a		