Effentora

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
PSUSA/1369/ 202304	Periodic Safety Update EU Single assessment - fentanyl (transmucosal route of administration)	25/01/2024	27/03/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1369/202304.
IA/0065	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	12/01/2023	n/a		

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
IG/1561	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	18/11/2022	n/a		
WS/2212	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. RMP update version 5.3 in order to reformat the RMP according to the revised guidance on GVP Module V (revision 2) and to implement PRAC comments arising from previous assessments as follows: - Revision of the list of safety concerns; - Implementation of key messages in educational materials adopted by PRAC for Instanyl; - Revision of Annex 6 to include verbatim the text adopted by PRAC for Instanyl as presented in Annex 2 of the PRAC PSUSA AR; - Revision of the use of digital access to educational material; - Explanation of the role of the Health Products Regulatory Authority (HPRA)'s CAPA being no longer found to be a trigger of the current RMP update. The 'additional risk minimisation measures' in the Annex II of the product information have been updated accordingly.	29/09/2022	09/10/2023	Annex II	Update of the RMP version 5.3 to implement PRAC conclusions of previous assessments.

	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				
IB/0063	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	22/04/2022	12/08/2022	SmPC and PL	Update of section 4.5 of the SmPC to include gabapentinoids as CNS depressant agents producing additive depressant effects in case of concomitant use with fentanyl-containing transdermal patches. The PL has been updated accordingly.
IB/0062	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	24/02/2022	12/08/2022	Labelling	Update of Annex IIIA (outer carton) of the PI by adding statements to ensure mitigation of risks related to the concerns raised regarding off-label use, misuse and accidental exposure to fentanyl products (transmucal route of administration).
IAIN/0061	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	07/01/2022	12/08/2022	Annex II and PL	
IAIN/0059/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a	09/08/2021	n/a		

	manufacturing site for the FP - Secondary packaging site				
IB/0057	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	21/07/2021	12/08/2022	SmPC and PL	
PSUSA/1369/202004	Periodic Safety Update EU Single assessment - fentanyl (transmucosal route of administration)	28/01/2021	07/04/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1369/202004.
II/0054/G	This was an application for a group of variations. Update of the SmPC in line with the recent PSUSA evaluation outcome and to reflect the updated Company core safety information. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/07/2020	07/04/2021	SmPC and PL	Section 4.4 has been updated to strengthen the warning regarding fentanyl's liability to abuse and dependence and add information on endocrine effects. For more information, please refer to the Summary of Product Characteristics.
IA/0055	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	08/07/2020	n/a		

IA/0053/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	12/03/2020	n/a		
IB/0052	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	23/08/2019	28/08/2020	SmPC and PL	
IAIN/0051	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	21/11/2018	n/a		
IB/0050	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	24/10/2018	n/a		
WS/1273/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.4 and 4.5 of the SmPC in order	31/05/2018	06/06/2019	SmPC and PL	Section 4.4 and 4.5 of the SmPC have been updated in order to introduce a warning on the risks of concomitant administration with benzodiazepines or related drugs which may result in profound sedation, respiratory depression, coma, and death. Additional recommendations are included to recommend that patients should be closely monitored for

	to add a warning on the interaction of fentanyl with benzodiazepines or other CNS depressants including alcohol following an internal cumulative review. The Package Leaflet is updated accordingly. Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on Hyperalgesia following an internal cumulative review. The Package Leaflet is updated accordingly. The wording proposals related to hyperalgesia are in line with the most recent CHMP opinion on PSUSA/00001369/201704. In addition, the MAH took the opportunity to introduce editorial and format changes in the SmPC and PL as well as to introduce information in the PL for serotonin syndrome, anaphylaxis and dose review for patients over 65 years in line with the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				signs and symptoms of respiratory depression and sedation in case of concomitant use of Effentora with benzodiazepines or related drugs. In addition, SmPC section 4.2 and 4.4 have been updated in order to indicate that in absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered and to warn that in case of insufficient pain control in response to an increased dose of fentanyl, the possibility of opioid-induced hyperalgesia should be considered. A fentanyl dose reduction or discontinuation of fentanyl treatment or treatment review may be indicated. The wording proposals related to hyperalgesia are in line with the most recent CHMP opinion on PSUSA/00001369/201704 from February 2018 and were implemented as part of procedure PSUSA/00001369/201704. The PL has been updated accordingly. In addition, the MAH took the opportunity to introduce editorial and format changes in the SmPC and PL as well as to introduce information in the PL for serotonin syndrome, anaphylaxis and dose review for patients over 65 years in line with the SmPC.
PSUSA/1369/201704	Periodic Safety Update EU Single assessment - fentanyl (transmucosal route of administration)	22/02/2018	08/05/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1369/201704.
IAIN/0049/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of	27/04/2018	n/a		

	manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IAIN/0048	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	16/01/2018	n/a		
II/0045	Update of sections 4.4 and 4.5 of the SmPC in order to add a warning on increased risk of depressant effects with the concomitant use of alcohol or other CNS depressants (e.g. opioids, sedatives or hypnotics, general anaesthetics, phenothiazines, tranquillisers, skeletal muscle relaxants, sedating antihistamine) with the possibility of a fatal outcome following a cumulative review on spontaneous reporting and literature review of this risk. The package leaflet has been updated accordingly. In addition, the marketing authorisation holder took the opportunity to introduce editorial clarifications in Annex I and Annex IIIB and changes in accordance to QRD template 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	09/03/2017	30/01/2018	SmPC and PL	This variation has led to updates to section 4.4 and section 4.5 in order to add a warning on increased risk of depressant effects with the concomitant use of alcohol or other CNS depressants (e.g. opioids, sedatives or hypnotics, general anaesthetics, phenothiazines, tranquillisers, skeletal muscle relaxants, sedating antihistamine) with the possibility of a fatal outcome following a cumulative review on spontaneous reporting and literature review of this risk. The package leaflet has been updated accordingly.
II/0044	Update of sections 4.4, 4.6 and 4.8 as applicable of the SmPC in order to add a warning on adrenal	15/12/2016	30/01/2018	SmPC, Annex II, Labelling	Update of sections 4.6 and 4.8 of the SmPC with neonatal opioid withdrawal syndrome, and sections 4.8 and 5.1 of

	insufficiency, androgen deficiency and Neonatal withdrawal syndrome following a request from FDA to introduce a class label safety warning. The PL was updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to apply a combined SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data			and PL	the SmPC regarding adrenal insufficiency and androgen deficiency following cumulative review of spontaneous reports and literature review. The PL was updated accordingly.
IAIN/0043	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	27/07/2016	n/a		
IB/0042	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	07/06/2016	n/a		
IA/0040	A.7 - Administrative change - Deletion of manufacturing sites	15/03/2016	n/a		
IA/0039	A.7 - Administrative change - Deletion of manufacturing sites	31/07/2015	n/a		
II/0037	Submission of the final study report of Post-authorisation safety study (PASS) - national descriptive and longitudinal study of patients treated with Effentora in France. The RMP version 4.0 has	23/07/2015	n/a		

	been updated accordingly. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IB/0038	B.III.1.z - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Other variation	14/07/2015	n/a		
T/0036	Transfer of Marketing Authorisation	12/02/2015	19/03/2015	SmPC, Labelling and PL	
PSUSA/1369/ 201404	Periodic Safety Update EU Single assessment - fentanyl (transmucosal route of administration)	18/12/2014	05/03/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1369/201404.
IB/0035	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/11/2014	n/a		
IB/0031/G	This was an application for a group of variations. B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition) B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its	13/08/2014	n/a		

	corresponding test method				
IA/0032	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	29/07/2014	n/a		
IAIN/0030	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	02/07/2014	n/a		
II/0026	Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on anaphylaxis and hypersensitivity, and to add hypersensitivity as a rare adverse reaction. Furthermore, the MAH took the opportunity to implement editorial changes with this variation. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	20/03/2014	05/03/2015	SmPC, Annex II and PL	Further to the assessment of post-marketing reports, as well as literature data, the CHMP proposed to update the safety information to include a warning on anaphylaxis and hypersensitivity, and to add hypersensitivity as a rare adverse reaction. The Package Leaflet was changed accordingly, and now includes the following text under 'Possible Side Effects' "Allergic reactions such as rash, redness, swollen lip and face, hives".
IA/0029/G	This was an application for a group of variations. B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	17/03/2014	n/a		
PSUSA/1369/	Periodic Safety Update EU Single assessment -	19/12/2013	28/02/2014	SmPC and PL	Refer to the Scientific conclusions and grounds

201304	fentanyl (transmucosal route of administration)				recommending the variation to the terms of the marketing authorisation for PSUSA/1369.
IAIN/0025	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/07/2013	n/a		
IAIN/0024/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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 B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	24/06/2013	28/02/2014	Annex II and PL	
IAIN/0023/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	21/02/2013	n/a		

	site				
R/0019	Renewal of the marketing authorisation.	13/12/2012	20/02/2013	SmPC, Annex II, Labelling and PL	Reviewing the efficacy and safety data available for Effentora since the granting of the marketing authorisation revealed no new major safety concerns. From the clinical perspective the CHMP considered that the overall benefit-risk ratio of Effentora remained unchanged and was positive. The CHMP was of the opinion that the renewal could be granted with unlimited validity.
IA/0022/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	08/02/2013	n/a		
T/0020	Transfer of Marketing Authorisation	20/11/2012	20/12/2012	SmPC, Labelling and PL	
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/05/2012	20/12/2012	PL	Update of the local representatives contact details in Annex IIIB.
IB/0016	C.I.8.b - Introduction of a new Pharmacovigilance system - which has been assessed by the relevant NCA/EMA for another product of the same MAH	02/03/2012	n/a		As Cephalon Europe is now a company part of the group Teva, the Pharmacovigilance System of Teva Europe will apply to Effentora. This Pharmacovigilance System has

					already been assessed by the EMA for other products of the Teva group. This change also implies that Dr Wendy Huisman is the new Qualified Person for Pharmacovigilance in the European Economic Area for Effentora.
II/0014	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. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	20/10/2011	22/11/2011	SmPC and PL	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. Updated SmPC and PL are as follows: 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. [...] Respiratory depression 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 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.

					PL Section 4 (possible side effects) Effentora like other fentanyl products can cause very severe breathing problems which can lead to death.
IA/0015/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site A.7 - Administrative change - Deletion of manufacturing sites 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) 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	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	This was an application for a group of variations. 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	26/08/2010	n/a	Annex II	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

	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), appendices and annex was also made. C.I.9.z - Changes to an existing pharmacovigilance system as described in the DDPS - Other variation C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV				sections (Procedure, Database, Contractual Arrangements and Quality Management), appendices and annex were also updated.
IA/0012/G	This was an application for a group of variations. 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	23/08/2010	n/a	Annex II and PL	
N/0010	The Marketing Authorisation Holder (MAH) took the opportunity to update the local representative for Portugal. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/07/2010	n/a	PL	
IB/0009	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	25/01/2010	n/a	SmPC	
II/0005	Update of section 5.3 of the SPC following	24/09/2009	10/12/2009	SmPC	The MAH submitted the results of new studies and section

	completion of new carcinogenicity and developmental/reproductive studies. Update of Summary of Product Characteristics				5.3 was updated accordingly. A reference was included to a male-mediated effect in fertility and early embryonic development in rats at high doses. A reference was also included on the findings related to 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/0004	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. Update of Summary of Product Characteristics and Package Leaflet	24/09/2009	10/12/2009	SmPC and PL	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.
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,	24/09/2009	10/12/2009	SmPC, Annex II and 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.

	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				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 updated 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	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	16/09/2009	n/a		
IA/0007	IA_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	IA_08_a_Change in BR/QC testing - repl./add. of	08/01/2009	n/a		

	batch control/testing site				