Zypadhera

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
IAIN/0054/G	This was an application for a group of variations. 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 -	24/10/2024		Annex II and PL	

[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).

	Not including batch control/testing 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 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				
IB/0052	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	29/07/2024	n/a		
IA/0053	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	16/07/2024	n/a		
IB/0051/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products A.7 - Administrative change - Deletion of	03/06/2024	n/a		

	manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place				
T/0050	Transfer of Marketing Authorisation	04/01/2024	08/02/2024	SmPC, Labelling and PL	
IB/0049	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	04/09/2023	n/a		
PSUSA/10540 /202203	Periodic Safety Update EU Single assessment - olanzapine	01/12/2022	n/a		PRAC Recommendation - maintenance
N/0047	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2021	08/02/2024	PL	
IA/0046	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	26/05/2021	n/a		
IAIN/0045	B.III.2.a.1 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS	11/12/2020	n/a		
IA/0044	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	30/11/2020	n/a		

	Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
WS/1956	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	19/11/2020	22/11/2021	SmPC, Annex II and PL	
IAIN/0042/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	20/08/2020	n/a		
PSUSA/10540 /201903	Periodic Safety Update EU Single assessment - olanzapine	12/12/2019	18/02/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10540/201903.
IAIN/0041	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	02/10/2019	n/a		
IA/0040/G	This was an application for a group of variations.	14/08/2019	n/a		

	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place				
IAIN/0038	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	10/12/2018	25/02/2019	PL	
WS/1454	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update section 4.8 of the SmPC to add stuttering as adverse drug reaction based on data from clinical trials and spontaneous reporting. PL is updated accordingly. In addition, the MAH took this opportunity to revised wording of section 5.2 on pharmacokinetics of olanzapine in hepatically impaired patients to improve clarity. In addition, the list of local representatives in the PL is being revised. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/11/2018	25/02/2019	SmPC and PL	Based on post-marketing cases and frequency of stuttering reported during clinical trials, plausible mechanism and causality linked with olanzapine use, the adverse event ' stuttering' is added to section 4.8 of the SmPC. The PL has been updated accordingly. In addition, the text in section 5.2 regarding the pharmacokinetics of olanzapine in hepatically impaired patients has be revised to reflect correctly data from the related study.

IB/0036	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	28/08/2018	n/a		
IA/0037/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	09/08/2018	n/a		
IG/0898	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	12/02/2018	25/02/2019	Annex II	
WS/1127	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO	23/02/2017	18/09/2017	SmPC and PL	

	new additional data is required to be submitted by the MAH				
II/0032	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/12/2016	n/a		
PSUSA/2206/201603	Periodic Safety Update EU Single assessment - olanzapine pamoate	27/10/2016	n/a		PRAC Recommendation - maintenance
WS/0987	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/09/2016	18/09/2017	SmPC, Annex II, Labelling and PL	
N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/04/2016	18/09/2017	PL	
IG/0662	A.1 - Administrative change - Change in the name and/or address of the MAH	23/02/2016	13/04/2016	SmPC, Labelling and PL	
IAIN/0027	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	14/10/2015	13/04/2016	SmPC, Labelling and PL	
IA/0026	A.7 - Administrative change - Deletion of manufacturing sites	23/04/2015	13/04/2016	Annex II and PL	

PSUV/0024	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance
IB/0025	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	14/08/2014	n/a		
IG/0455	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	08/07/2014	05/05/2015	Annex II and PL	
II/0022	Update of sections 4.4 and 5.1 of the SmPC in order to reflect the level of data available in adolescents with bipolar I disorder (manic or mixed episodes) or schizophrenia following the completion of a long-term safety study, in fulfilment of the requirement laid down in Article 46 of the paediatric regulation. In addition, administrative updates to the reconstitution instructions in the SmPC and PL to align with information provided by the manufacture of the kit needles and syringes were proposed. The MAH took also the opportunity to implement editorial changes with this variation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/04/2014	05/05/2015	SmPC, Labelling and PL	Please refer to the scientific discussion Zypadhera-H-000890-II-0022-AR.
IB/0021	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting	13/09/2013	n/a		

	material/intermediate/reagent - Other variation				
R/0019	Renewal of the marketing authorisation.	27/06/2013	26/08/2013	SmPC, Annex II, Labelling and PL	Based on the review of the cumulative efficacy and safety data available from clinical trials, post-marketing studies and spontaneous reports as well as the scientific literature, the CHMP concluded that there were no changes to the known benefits and safety concerns associated with Zypadhera when used in the approved indication. The CHMP therefore concluded that the benefit/risk balance of Zypadhera as maintenance treatment of adult patients with schizophrenia remained favourable and recommended the renewal of the marketing authorisation with unlimited validity.
IG/0337	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	09/08/2013	n/a		
WS/0337	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.8 of the SmPC and relevant section of the PL to include "amnesia, epistaxis, abdominal distension, arthralgia, GGT high, uric acid high, pyrexia and dysarthria", as new undesirable effects for Zyprexa, Zyprexa Velotab and Zypadhera and "injection site abscess and injection site pain" as new undesirable effects for Zypadhera. The frequencies of currently labelled undesirable effects have also been revised throughout sections 4.4 and 4.8 of the SmPC and relevant sections of the	25/04/2013	27/05/2013	SmPC and PL	Lilly has recently completed the process of integration of 42 controlled olanzapine clinical studies into a single Olanzapine Integrated Database of patients exposed to olanzapine across multiple indications and formulations. The Olanzapine Integrated Database aimed at creating a sufficiently large database with maximum olanzapine exposure numbers in adults as possible, while maintaining the characteristics that would make the results of the studies consistent enough to be rationally combined for a robust analysis of safety. Following an analysis of safety data from the Olanzapine Integrated Database, the MAH proposed an update the Product information to include amnesia, epistaxis, abdominal distension, arthralgia, GGT high, uric acid high,

	PL. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				pyrexia and dysarthria", as new undesirable effects for Zyprexa, Zyprexa Velotab and Zypadhera and "injection site abscess and injection site pain" as new undesirable effects for Zypadhera. The frequencies of currently labelled undesirable effects have also been revised throughout sections 4.4 and 4.8 of the SmPC and relevant sections of the PL.
II/0018	Update of sections 4.2 and 4.4 of the SmPC to remove the requirement for patient accompaniment following the administration of Zypadhera, to update the information on post-injection syndrome, and to reinforce instructions for physicians to check for symptoms of post injection syndrome before the patient leaves the health care facility. The Package Leaflet and Annex II have 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	21/02/2013	27/05/2013	SmPC, Annex II and PL	There has been no confirmed post-injection-syndrome event that has occurred more than 3 hours after the injection since the marketing of Zypadhera. As the majority of post-injection syndrome events occur within 1 hour of receiving the injection of Zypadhera and the patients are observed for 3 hours after receiving the injection, the chances of a post-injection event occurring in the period after leaving the health care facility and while the patient is being accompanied to their destination can be seen to be very low. Therefore, the requirement for doctors or nurses to ensure that patients will not travel alone to their destination after injection has been removed.
IA/0016	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)	07/08/2012	n/a		
IA/0015	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)	12/07/2012	n/a		

WS/0215	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update to section 4.8 of the olanzapine SmPCs to add urinary retention as an undesirable effect and to reflect this change in the section 4 of the PLS further to a cumulative review of "urinary retention" in temporal association with olanzapine treatment as requested by the CHMP following assessment of PSUR 25. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	24/05/2012	27/06/2012	SmPC, Annex II, Labelling and PL	Further to the assessment of safety data, the Product Information (section 4.8 of the SmPC and section 4 of the PL) has been updated to add loss of ability to urinate as an uncommon side-effect in patients taking olanzapine.
IA/0014	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	21/02/2012	n/a		
WS/0127	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC section 4.4 to include metabolic monitoring frequency examples following the assessment of the latest PSURs and RMP. The Package Leaflet is updated accordingly. Update of the frequency of Venous thromboembolism (VTE) in SmPC section 4.4 and 4.8 following PhVWP recommendation to include warnings about the risk	20/10/2011	24/11/2011	SmPC and PL	Further to the assessment of safety data, the Product Information (section 4.4 of the SmPC and section 2 of the PL) has been updated to add examples of monitoring of blood glucose, lipids, weight in patients taking olanzapine. In addition warning on the risk of blood clotting (venous thromboembolism) was made consistent throughout Zyprexa products. The frequency of VTE was also recalculated and as a result assessed as uncommon in SmPC sections 4.4 and 4.8 and PL section 4. Last, the PL of Zyprexa IM rapid-acting injection (RAIM Zyprexa) was updated to provide information on the use

	of venous thromboembolism. The Package Leaflet is updated accordingly. The Package Leaflet is brought in line with the SmPC wording to include the use of tranquillisers and benzodiazepines for Zyprexa IM rapid-acting injection (RAIM). Correction to the annexes for Zyprexa coated tablets, specifically the excipient constituents of the edible blue ink of the 2.5-, 5-, 7.5-, and 10-mg tablet coating in the respective SmPCs and PL is aligned with information in Module 3 of the dossier. C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH				of tranquillisers and benzodiazepines which is in line with the SmPC.
WS/0182	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Following PhVWP/CHMP conclusions of June 2011, update of the Summary of Product Characteristics (SmPC) and Package Leaflet (PL) regarding the use of antipsychotics during the third trimester of pregnancy and risk of abnormal muscle movements and/or withdrawal symptoms in newborns in accordance with the PhVWP/CHMP class labelling recommended wording. C.I.3.b - Implementation of change(s) requested	22/09/2011	20/10/2011	SmPC and PL	There is evidence to suggest that the newborn babies of mothers treated with antipsychotics during the third trimester of pregnancy may suffer adverse effects (primarily extrapyramidal side effects and/or withdrawal effects). Whilst there is limited data available for some antipsychotics, this is likely to be a class effect. In addition to the inclusion of neonatal drug withdrawal syndrome as listed adverse reaction, section 4.6 of the SmPC and section 2 of the PL were updated in accordance with the PhVWP/CHMP class labelling recommended wording, as follows: SmpC: Neonates exposed to antipsychotics (including [olanzapine]) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or

	following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. PL: The following symptoms may occur in newborn babies, of mothers that have used [olanzapine] in the last trimester (last three months of their pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding. If your baby develops any of these symptoms you may need to contact your doctor.
IA/0009/G	This was an application for a group of variations. 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) 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	14/06/2011	n/a		
IA/0008	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	25/02/2011	n/a	Annex II	
IB/0007	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	08/02/2011	n/a		

	or addition) for the AS or a starting material/intermediate				
IB/0006	B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue	08/02/2011	n/a		
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/12/2010	n/a	PL	
WS/0021	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008, update of sections 4.4 (deletion of a sentence in the warning related to hepatic function) and 4.8 (modification of the prolactin information in the footnote) of the Summary of Product Characteristics resulting of a review of the company core data sheet. Additional changes were made to the Product Information and Annex II in accordance with the QRD templates (version 7.3.1) and contact details of the local representatives (France, United Kingdom) were also updated in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-	22/07/2010	01/09/2010	SmPC, Annex II and PL	Based on updated analyses concerning liver enzymes elevations and prolactin levels provided by the Marketing Authorisation Holder, the CHMP considered that the recommendation regarding dose reduction in patients with elevated liver enzymes and the reference to a decrease of prolactin levels over time related to diagnosis were no longer appropriate and recommended to delete this information. Subsequently, section 4.4 and footnote of section 4.8 were updated accordingly.

	clinical, clinical or pharmacovigilance data				
II/0004	Update of the section 4.4 of the Summary of Product Characteristics to include a warning on sudden cardiac death. In addition, section 4.8 is also updated to include urinary incontinence as an uncommon adverse drug reaction and to revise the information on elevated plasma prolactin concentrations and related clinical manifestations. Section 4 of the Package Leaflet has been amended accordingly. Details of the local representative in Spain were updated in the Package Leaflet. Additionally, the incidence of post-injection syndrome was updated in section 4.4 and editorial changes were made in the relevant sections of the Product Information. Update of Summary of Product Characteristics and Package Leaflet	19/11/2009	21/12/2009	SmPC and PL	Following review of the latest safety information for olanzapine provided by the MAH on sudden cardiac death, urinary incontinence, elevated plasma prolactin concentrations and related clinical manifestations and post-injection syndrome, the CHMP considered that: - In postmarketing reports with olanzapine, the events of sudden cardiac death have been reported in patients with olanzapine.In a retrospective observational cohort study, the risk of presumed sudden cardiac death in patients treated with olanzapine was approximately twice the risk in patients not using antipsychotics. In the study, the risk of olanzapine was comparable to the risk of atypical antipsychotics included in a pooled analysis. Subsequently, this information was reflected as a warning in section 4.4. - Two apparently unconfounded serious case reports, and 13 serious case reports of urinary incontinence with a positive dechallenge were reported in PSUR 23. According to the current SPC, olanzapine exhibits a range of receptor affinities (Ki; < 100 nM) including ?1-adrenergic receptors. Furthermore; in the clinical trial data (from adult placebo-controlled database) the frequency of urinary incontinence with olanzapine was 0.3% (i.e., uncommon). Subsequently, urinary incontinence was added in section 4.8 as uncommon ADR. - In clinical trials of up to 12 weeks, plasma prolactin concentrations exceeded the upper limit of normal range in approximately 30% of olanzapine treated patients with normal baseline prolactin value. In the majority of these patients the elevations were generally mild, and remained

					below two times the upper limit of normal range. In patients with schizophrenia, mean prolactin level changes decreased with continued treatment, whereas mean increases were seen in patients with other diagnoses. The mean changes were modest. Generally in olanzapine-treated patients potentially associated breast- and menstrual related clinical manifestations (e.g. amenorrhoea, breast enlargement,
II/0002	Update of the section 4.8 of the Summary of Product Characteristics (SPC) to provide further detailed information on the risk of weight gain following CHMP conclusions on additional analyses performed by the MAH. Safety information on glucose levels observed during long term exposure was also updated. Editorial change was made in section 4.4 of the SPC. Furthermore, section 6.6 of the SPC and relevant section of the Package Leaflet were amended following CHMP review on the information related to instructions for use of the needles. Changes to the Product Information in line with latest QRD templates were also made. Update of Summary of Product Characteristics	29/05/2009	27/07/2009	SmPC and PL	Following further analyses related to weight, lipids, and glucose for two populations (elderly patients with Alzheimer's disease, other types of dementia, or Parkinson's disease; and patients who were naïve to antipsychotic treatment when they entered the relevant clinical trials) and additional weight analyses from 2 clinical studies (F1D-US- HGJU and F1D-HGGF) performed by the MAH, the CHMP recommended that an update of the SPC should be made in relation to the wording on weight gain in section 4.8 to provide better information for prescribers. The CHMP recommended that the frequency of potentially clinically significant weight gain should be clarified as proportions of patients in each class (over 7%, over 15% and over 25% weight gain) in short term use (under 24 weeks) and long term use (over 24 weeks), separately. In line with the CHMP's recommendations, the MAH updated footnotes 1 and 9 as follows: Adults Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Following short term treatment (median duration 47 days), weight gain ? 7% of baseline body weight was very common (22.2%), ?

					15 % was common (4.2 %) and ? 25 % was uncommon (0.8 %). Patients gaining ? 7 %, ? 15 % and ? 25 % of their baseline body weight with long-term exposure (at least 48 weeks) were very common (64.4 %, 31.7 % and 12.3 % respectively). Adolescents Following short term treatment (median duration 22 days), weight gain ? 7 % of baseline body weight (kg) was very common (40.6 %), ? 15 % of baseline body weight was common (7.1 %) and ? 25 % was common (2.5%). With long-term exposure (at least 24 weeks), 89.4 % gained ? 7 %, 55.3 % gained ? 15 % and 29.1 % gained ? 25 % of their baseline body weight.
IA/0003	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	18/06/2009	n/a	SmPC and PL	
IA/0001	IA_43_a_01_ Add./replacement/del. of measuring or administration device - addition or replacement	15/12/2008	n/a	SmPC, Labelling and PL	