Latuda

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
IA/0042	A.7 - Administrative change - Deletion of manufacturing sites	09/01/2024		Annex II and PL	
IB/0040/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release	08/08/2023	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).

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	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products				
IA/0039	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	10/11/2022	n/a		
IA/0038	A.7 - Administrative change - Deletion of manufacturing sites	21/10/2022	n/a		
II/0037	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	10/03/2022	n/a		
II/0036	Update of section 4.8 of the SmPC to amend the frequency of ADRs in adults and to add 'syncope' (frequency uncommon) and 'cerebrovascular accident' (frequency rare) following the assessment of the procedure EMEA/H/C/PSUSA/00010114/202010. The Package	02/12/2021	18/11/2022	SmPC, Labelling and PL	

	Leaflet is updated accordingly. Minor adjustments of the PTs based on the MedDRA definitions were implemented and the ADR 'blood creatine phosphokinase increased' was moved to the SOC Investigations. In addition, the marketing authorisation holder has taken the opportunity to combine all the dosages in a single version of the SmPC, to update the list of local representatives in the PL and to bring the PI in line with the latest QRD template version 10.2 Rev. 1. 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				
PSUSA/10114 /202010	Periodic Safety Update EU Single assessment - lurasidone	10/06/2021	n/a		PRAC Recommendation - maintenance
II/0033	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	11/03/2021	n/a		
IA/0035	A.7 - Administrative change - Deletion of manufacturing sites	02/03/2021	25/10/2021	Annex II and PL	
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/01/2021	25/10/2021	PL	
II/0029	Extension of Indication for the treatment of	23/07/2020	25/08/2020	SmPC and PL	Please refer to Scientific Discussion 'Latuda-H-C-2713-II-

	schizophrenia in adolescent from 13 years and over; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 8.1 of the RMP has also been agreed. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest excipient guideline. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				Var.29'.
IB/0031	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/08/2020	25/10/2021	SmPC and PL	
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/03/2020	25/08/2020	PL	
IAIN/0028	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	23/10/2019	n/a		
N/0027	Minor change in labelling or package leaflet not	16/07/2019	17/10/2019	PL	

	connected with the SPC (Art. 61.3 Notification)				
IAIN/0026	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	18/03/2019	17/10/2019	Annex II and PL	
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/01/2019	17/10/2019	PL	
II/0022	Update of section 4.5 of the SmPC in order to update the safety information following literature review regarding drug interaction between a strong CYP3A4 inhibitor (i.e.posaconazole) and lurasidone. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/12/2018	17/10/2019	SmPC	Further to the review of literature data where 11 healthy subjects were coadministered lurasidone and posaconazole (strong CYP3A4 inhibitor) resulting in an approximate 4-5 fold increase in lurasidone exposure and a persistent effect of posaconazole on lurasidone (up to 2-3 weeks after stop of co-administration), the CHMP agreed to update the SmPC of Latuda in order to reflect new drug interactions between a strong CYP3A4 inhibitor (i.e.posaconazole) and lurasidone.
R/0020	Renewal of the marketing authorisation.	20/09/2018	14/11/2018	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Latuda in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IAIN/0024/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	23/10/2018	n/a		

	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site				
IAIN/0023	B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	23/10/2018	17/10/2019	Annex II and PL	
II/0021	Update of sections 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMEA/H/C/002713/P46/008). In addition, section 4.2 of the SmPC has been updated to cross refer to section 5.1. 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	18/10/2018	17/10/2019	SmPC	For study D1050326 the primary efficacy endpoint was defined as the mean change from baseline to Week 6 in Children's Depression Rating Scale, Revised (CDRS-R) Total Score. The key secondary endpoint was Clinical Global Impression – Bipolar Version, Severity of Illness (CGI-BP-S) Depression Score. Statistically significant differences favouring lurasidone over placebo were shown for these endpoints for the total population studied, beginning at Week 2 and were maintained at each study visit through to the end of the study. However, the primary and key secondary efficacy endpoints were not met in younger patients (below 15 years of age). The safety profile of lurasidone in children included in this short-term study is in general consistent with that observed when treated within the approved indication in adults, however, differences in frequency of the most commonly occurred adverse reactions have been observed in paediatric patients for nausea (very common), diarrhoea (common) and decreased appetite (common), compared with adults (common, unknown, and uncommon, respectively). Based on these paediatric data sections 4.2 and 5.1 of the SmPC have been updated accordingly.

PSUSA/10114 /201710	Periodic Safety Update EU Single assessment - lurasidone	17/05/2018	n/a		PRAC Recommendation - maintenance
T/0019	Transfer of Marketing Authorisation	21/02/2018	12/03/2018	SmPC, Labelling and PL	
PSUSA/10114 /201610	Periodic Safety Update EU Single assessment - lurasidone	18/05/2017	13/07/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10114/201610.
II/0016	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/07/2017	n/a		
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/05/2017	12/03/2018	PL	
PSUSA/10114 /201510	Periodic Safety Update EU Single assessment - lurasidone	13/05/2016	n/a		PRAC Recommendation - maintenance
IAIN/0014/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.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	10/03/2016	22/03/2017	Annex II and PL	

T/0013	Marketing Authorisation transfer from Takeda Pharma A/S to Sunovion Pharmaceuticals Europe Ltd. Transfer of Marketing Authorisation	28/01/2016	15/02/2016	Labelling and PL	
PSUSA/10114 /201504	Periodic Safety Update EU Single assessment - lurasidone	19/11/2015	11/01/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10114/201504.
IAIN/0011	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	08/01/2016	n/a		
IAIN/0010	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	10/12/2015	n/a		
II/0009	Update of section 4.8 of the SmPC to include the ADR Stevens-Johnson Syndrome, and to include information regarding serious cases of skin and other hypersensitivity reactions reported in the post-marketing setting. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make a minor correction in section 5.1 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/10/2015	11/01/2016	SmPC and PL	Post marketing reports of clinically serious cases of skin and other hypersensitivity reactions have been reported in association with lurasidone treatment, including some reports of Stevens-Johnson syndrome.

IB/0008	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	08/09/2015	11/01/2016	SmPC and PL	
IA/0006/G	This was an application for a group of variations. 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 B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	24/07/2015	n/a		
PSUSA/10114 /201410	Periodic Safety Update EU Single assessment - lurasidone	21/05/2015	17/07/2015	SmPC and PL	Please refer to Latuda-PSUSA-00010114-201410 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
II/0003/G	This was an application for a group of variations. Update of section 5.2 of the SmPC with new CYP	26/03/2015	17/07/2015	SmPC	In vitro, lurasidone demonstrated no direct, or weak inhibition (direct or time-dependent) (IC50>5.9 µM) of the enzymes cytochrome P450 (CYP)1A2, CYP2B6, CYP2C8,

	inhibition data based on three non-clinical in vitro studies (GE-1267/GE-1284-G, AE-7394-G and PCA 14340) undertaken to fulfil post-authorisation measures (RECs) agreed at the time of the initial MAA. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. Based on this data, lurasidone is not expected to affect the pharmacokinetics of medicinal products that are substrates of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, and CYP2E1.
IB/0005	To update sections 4.2 and 5.2 of the SmPC to include data from study D1050300 on the approved lurasidone PIP for schizophrenia. In addition the MAH took this opportunity to update the local representatives in Greece and Finland. Finaly, minor editorial amendments were performed in the annexes of the following languages: CS, DA, DE, FR, PT, NO and SV 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	18/02/2015	17/07/2015	SmPC and PL	
PSUV/0002	Periodic Safety Update	20/11/2014	15/01/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending

					the variation to terms of the Marketing Authorisation(s)' for PSUV/0002.
IB/0001	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	04/07/2014	15/01/2015	SmPC, Labelling and PL	