Mysimba

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
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/07/2018		PL	
PSUSA/10366 /201709	Periodic Safety Update EU Single assessment - naltrexone / bupropion	26/04/2018	02/07/2018	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10366/201709.
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/03/2018	02/07/2018	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).

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II/0023	Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the dosage recommendation and safety information for patients with moderate renal impairment based on final results from study NaltrexBuprop-1006 - A Phase 1, Open-Label, Parallel Study to Evaluate the Pharmacokinetics of a Single Oral Dose of Extended-Release Combination of Naltrexone and Bupropion in Subjects With Normal Renal Function or Varying Degrees of Impaired Renal Function. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/12/2017	26/01/2018	SmPC and PL	The SmPC sections 4.2, 4.3, 4.4, 4.8 and 5.2 has been updated in order to update the dosage recommendation and safety information for patients with moderate renal impairment based on final results from study NaltrexBuprop-1006 - A Phase 1, Open-Label, Parallel Study to Evaluate the Pharmacokinetics of a Single Oral Dose of Extended-Release Combination of Naltrexone and Bupropion in Subjects With Normal Renal Function or Varying Degrees of Impaired Renal Function. The proposed update removes the contraindication for patients with severe renal impairment, provides new information on the posology and additional warning that the maximum recommended daily dose for naltrexone / bupropion should be reduced for this patient population. The PL have been updated accordingly.
PSUSA/10366 /201703	Periodic Safety Update EU Single assessment - naltrexone / bupropion	12/10/2017	08/12/2017	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10366/201703.
IB/0026	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)	05/12/2017	26/01/2018	SmPC	
IB/0024	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	09/11/2017	n/a		
IB/0022/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.z - Change in the manufacturer of AS or of a	11/10/2017	n/a		

	starting material/reagent/intermediate for AS - Other variation B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0021	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	21/09/2017	08/12/2017	SmPC, Labelling and PL	
II/0017	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/09/2017	n/a		
N/0020	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/09/2017	08/12/2017	PL	
IB/0018/G	This was an application for a group of variations. 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.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation	04/07/2017	n/a		

	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 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)				
PSUSA/10366 /201609	Periodic Safety Update EU Single assessment - naltrexone / bupropion	21/04/2017	23/06/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10366/201609.
II/0015	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	22/06/2017	n/a		
II/0014	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	22/06/2017	n/a		
II/0010	Update of sections 4.4 and 4.8 of the SmPC to update existing warnings on seizures and blood pressure increase and to include abdominal discomfort, anxiety, dyspepsia, fatigue, hallucination, headache, hypertension, insomnia, irritability, and rash as adverse drug reactions for the Naltrexone/ Bupropion combination with a frequency unknown based on the results of study NB-CVOT (a Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Assessing the Occurrence of Major Adverse Cardiovascular Events (MACE) in Overweight and	22/06/2017	08/12/2017	SmPC and PL	In a cardiovascular outcomes trial (CVOT) of patients at increased risk of a cardiovascular event, mean increases from baseline in systolic and diastolic blood pressure of approximately 1 mmHg compared to placebo were observed. This incidence of seizure, along with incidence of seizure in subjects who received naltrexone / bupropion at the time of interim analysis in a large, ongoing cardiovascular outcomes trial (CVOT), was no higher than the seizure rate with bupropion as a single agent at approved doses.

	Obese Subjects with Cardiovascular Risk Factors Receiving Naltrexone SR/Bupropion SR). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0013/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.d - Change in the batch size (including batch size ranges) of the finished product - The change relates to all other pharmaceutical forms manufactured by complex manufacturing processes B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	01/06/2017	n/a		

	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product				
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/03/2017	23/06/2017	PL	
II/0011	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	23/02/2017	n/a		
IAIN/0008/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.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.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms	09/11/2016	12/12/2016	SmPC	
PSUSA/10366 /201603	Periodic Safety Update EU Single assessment - naltrexone / bupropion	27/10/2016	n/a		PRAC Recommendation - maintenance
II/0005/G	This was an application for a group of variations. 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	15/09/2016	n/a		

	new additional data to be submitted by the MAH where significant assessment is required 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				
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/08/2016	12/12/2016	PL	
II/0003/G	This was an application for a group of variations. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	26/05/2016	n/a		
N/0004	Inclusion of the list of local representatives at the end of the package leaflet. In addition, the MAH took the opportunity to make linguistic amendments in the Bulgarian, Croatian, Czech, Hungarian, Lithuanian, Polish, Romanian, and Slovenian labelling and package leaflets. Minor change in labelling or package leaflet not	20/05/2016	12/12/2016	PL	

	connected with the SPC (Art. 61.3 Notification)				
PSUSA/10366 /201509	Periodic Safety Update EU Single assessment - naltrexone / bupropion	14/04/2016	n/a		PRAC Recommendation - maintenance
IAIN/0001	A.1 - Administrative change - Change in the name and/or address of the MAH	03/12/2015	12/12/2016	SmPC, Labelling and PL	