Vimpat

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
IB/0101	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	05/01/2024		SmPC 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).

IA/0102	A.7 - Administrative change - Deletion of manufacturing sites	08/12/2023	n/a		
WS/2515	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of an updated RMP version 17.0 in order to introduce new updates including the removal of category 3 study EP0158 due to study closure by lack of enrolment, and the removal of category 3 studies (SP848 and EP0034). 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	26/10/2023	n/a		
IB/0099/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size	03/02/2023	n/a		

	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer				
N/0098	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/10/2022		PL	
IB/0097/G	This was an application for a group of variations. 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 corresponding test method 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)	06/10/2022	n/a		
PSUSA/1816/202108	Periodic Safety Update EU Single assessment - lacosamide	22/04/2022	08/07/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1816/202108.
WS/2049/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. B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening	27/01/2022	04/03/2022	SmPC, Labelling and PL	

	(supported by real time data) C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IB/0095	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	29/11/2021	n/a		
IG/1447/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	18/10/2021	n/a		
IG/1416	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 corresponding test method	11/08/2021	n/a		
WS/2066	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 in order to add dyskinesia to the list of adverse drug reactions	10/06/2021	04/03/2022	SmPC, Labelling and PL	The available data indicate a possible association between dyskinesia and treatment with lacosamide although the number of assessable cases is low. Section 4.8 of the SmPC is being updated to add dyskinesia as an uncommon adverse reaction. For more information, please refer to the Summary of

	(ADRs) with frequency uncommon following the outcome of continuous safety signal assessments of the relevant reported clinical and post-marketing cases. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the PI, to bring it in line with the latest QRD template version 10.2 and relevant guidelines and to update the details of the UK local representative in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Product Characteristics.
WS/1782	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Extension of Indication to include the treatment as adjunctive therapy of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy for Lacosamide UCB and Vimpat. Consequently sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 15.1 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The MAH also takes the opportunity to align the PI of Lacosamide UCB with the PI of Vimpat.	15/10/2020	01/12/2020	SmPC and PL	Please refer to Scientific Discussion Vimpat-H-C-WS1782 and Lacosamide UCB-H-C-WS1782

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IG/1251	A.7 - Administrative change - Deletion of manufacturing sites	07/05/2020	n/a		
IB/0089	B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	30/04/2020	n/a		
WS/1748	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	16/01/2020	n/a		
IB/0087/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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 corresponding test method B.I.b.1.z - Change in the specification parameters	13/01/2020	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IG/1177	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	17/12/2019	n/a		
IG/1162	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	13/11/2019	n/a		
IG/1151	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	29/10/2019	n/a		
IB/0081/G	This was an application for a group of variations. B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	29/08/2019	03/09/2020	SmPC, Labelling and PL	

	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes				
II/0073/G	This was an application for a group of variations. Update of sections 4.2, 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR). In addition, the MAH took the opportunity to correct the frequency of the adverse event 'coordination abnormal' in section 4.8 of the SmPC from 'common' to 'uncommon' as the frequency of this ADR was erroneously classified as 'common' due to rounded ADR percentages in the initial SmPC. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted. 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	14/06/2019	31/07/2019	SmPC and PL	Based on available information from the UCB Global Safety database on serious cardiac arrhythmias in patients with status epilepticus treated with lacosamide, it is considered that the mere combination of status epilepticus and lacosamide treatment does not seem to bear an increased risk for serious arrhythmias as compared to what can be expected in status epilepticus, the underlying conditions of status epilepticus, and lacosamide treatment in general. However, there is some concern for serious arrhythmias with IV administration. In eight cases, the serious arrhythmia occurred during or in close temporal proximity to the infusion. Serious cardiac arrhythmias during or shortly after infusion of lacosamide may actually be especially problematic in non-status epilepticus patients since they are not necessarily monitored as rigorously as patients with refractory status epilepticus, and there may not be the same readiness to treat such life-threatening events outside the intensive care unit. Therefore, in order to ensure adequate detection of serious cardiac arrhythmias in patients not treated in the intensive care unit, serious cardiac arrhythmias is added to section 4.2 of the SmPC: Initiation of lacosamide with a loading dose: "It

					should be administered under medical supervision with consideration of the potential for increased incidence of serious cardiac arrhythmias and central nervous system adverse reactions (see section 4.8).” In patients who develop serious cardiac arrhythmia, clinical benefit/risk assessment should be performed and if needed lacosamide should be discontinued.
IAIN/0080	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	10/05/2019	n/a		
IB/0079	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/04/2019	n/a		
PSUSA/1816/ 201808	Periodic Safety Update EU Single assessment - lacosamide	11/04/2019	n/a		PRAC Recommendation - maintenance
IB/0078	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	26/03/2019	n/a		
IB/0077/G	This was an application for a group of variations. B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	04/01/2019	n/a		

IA/0075/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 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) B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	23/11/2018	n/a		
II/0074/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product	11/10/2018	n/a		
II/0070/G	This was an application for a group of variations.	26/07/2018	31/07/2019	SmPC, Labelling and	As concluded in procedure EMA/H/C/863/P46 028, final results from the study SP0969 showed that the efficacy

	Update of sections 4.8, 5.1, and 5.2 of the SmPC in order to update clinical efficacy and safety data in the paediatric population with the results from study SP0969: a phase 3, multicentre, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lacosamide as adjunctive therapy in subjects with epilepsy ≥4 years to <17 years of age with uncontrolled partial-onset seizures; 3 new ADRs (nasopharyngitis, pharyngitis, and pyrexia) have been added based on the results of the above mentioned study; Update of section 5.2 of the SmPC in order to update the pharmacokinetic data in the paediatric population based on results from the CL0430 population pharmacokinetic (PK) analyses; Update of section 4.8 of the SmPC in order to update the incidence of decreased appetite, lethargy, and abnormal behaviour in the paediatric population based on results from the updated safety data for Pool SPX-1 with clinical cut-off date of 01 November 2016. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI. The MAH also took the opportunity to revise Annex A as requested. 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			PL	results were in line with the known efficacy from studies conducted in adult population. These efficacy results in the pediatric population were reflected in section 5.1 and 5.2 of the SmPC. Based on the safety results, nasopharyngitis, pharyngitis and pyrexia were added in section 4.8 as new adverse reactions. The incidences of already listed adverse reactions in the paediatric population were updated. The analysis of updated data in Pool SPX-1 yielded results that were similar to those reported in the initial paediatric submission, with the following exceptions: decreased incidence of convulsion, decreased appetite, lethargy, and abnormal behaviour. Results from the CL0430 population pharmacokinetic analyses showed that no significant influence of race, ethnicity, sex, or estimated glomerular filtration rate (eGFR) on the clearance of lacosamide was identified. The results were reflected in section 5.2 of the SmPC.

	data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IA/0072/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size 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.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other	25/05/2018	n/a		

	variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0071	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	04/04/2018	n/a		
IA/0069/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size 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.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	14/12/2017	n/a		
IB/0068/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	21/11/2017	31/07/2019	SmPC, Annex II, Labelling and PL	

	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site 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 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.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.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s)				
II/0065/G	This was an application for a group of variations.	20/07/2017	14/09/2017	SmPC,	Please refer to the scientific discussion Vimpat

	Extension of Indication to extend the indication for Vimpat to monotherapy and adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adolescents and children aged 4 to less than 16 years with epilepsy. For the treatment initiation pack, the use was only extended to adolescents weighting 50 kg or more as it is not suitable for the weight-based dosing regimen recommended for patients weighing less. Sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2 and 5.3 of the SmPC have been updated including the addition of a warning of the potential for electro-clinical worsening in specific epileptic syndromes. The Package Leaflet was updated in accordance. Moreover, section 6.3 of the SmPC of the syrup is updated to reflect the extension of shelf life after first opening from 4 weeks to 2 months. Furthermore, a 10 mL dosing syringe for the 200 ml and the 465 ml syrup bottles is introduced as additional dosing device for paediatric population; section 6.5 of the SmPC of the syrup presentations is updated accordingly. Finally, the PI was also brought in line with the latest QRD template version and editorial amendments were made in several sections. The MAH also took the opportunity to introduce a combined SmPC for the film coated tablets. Moreover, updated RMP version 12.2 has been agreed. B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)			Labelling and PL	EMEA/H/C/000863/II/0065/G.

	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 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 C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IAIN/0067/G	This was an application for a group of variations. B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished	03/05/2017	14/09/2017	SmPC, Labelling and PL	

	product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes				
II/0066/G	This was an application for a group of variations. Update of section 4.2 of the SmPC in order to update the safety information regarding the use of lacosamide in patients with hepatic impairment, section 4.8 to add a new adverse drug reaction (hepatic enzyme increased (> 2x ULN)) and section 4.9 regarding lacosamide overdose based on postmarketing reports. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet for Lithuania, Latvia, Estonia, Portugal and Finland.	23/02/2017	24/03/2017	SmPC and PL	A maximum dose of 300 mg/day is recommended for patients with mild to moderate hepatic impairment. Lacosamide should be administered to patients with severe hepatic impairment only when the expected therapeutic benefits are anticipated to outweigh the possible risks. The dose may need to be adjusted while carefully observing disease activity and potential side effects in the patient. Symptoms observed after an accidental or intentional overdose of lacosamide are primarily associated with CNS and gastrointestinal system. Reactions reported after an intake of more than 800 mg are dizziness, nausea, vomiting, seizures (generalized tonic-clonic seizures, status epilepticus). Cardiac conduction disorders, shock and coma have also been observed. Fatalities have been reported in patients following an intake of acute single overdose of

	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 C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				several grams of lacosamide.
II/0060/G	This was an application for a group of variations. 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 B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	10/11/2016	12/12/2016	SmPC, Annex II, Labelling and PL	
II/0064/G	This was an application for a group of variations.	01/12/2016	n/a		

	B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IA/0062/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	21/07/2016	n/a		

	or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.7 - Administrative change - Deletion of manufacturing sites				
II/0061/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.5.e - Change to in-process tests or limits applied during the manufacture of the finished product - Widening of the approved IPC limits, which may have a significant effect on overall quality of the finished product B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	21/07/2016	n/a		
IB/0063	B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	20/07/2016	n/a		
PSUSA/1816/ 201508	Periodic Safety Update EU Single assessment - lacosamide	14/04/2016	n/a		PRAC Recommendation - maintenance
IB/0059	B.I.b.2.e - Change in test procedure for AS or	15/12/2015	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IA/0058/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.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	10/12/2015	n/a		
IA/0056/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites 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	16/10/2015	n/a		
IA/0055	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	20/07/2015	n/a		

IAIN/0053	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	08/06/2015	n/a		
IAIN/0054/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.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	03/06/2015	02/06/2016	Annex II and PL	
IB/0052	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	30/03/2015	n/a		
II/0051/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.b.1.f - Change in the specification parameters and/or limits of an AS, starting	26/02/2015	n/a		

	material/intermediate/reagent - Change outside the approved specifications limits range for the AS				
II/0050	Update of section 4.9 of the SmPC following a case report of cardiac arrest upon overdose and a MAH cumulative review of cardiac disorders or mortality following acute lacosamide overdose. The package leaflet is updated accordingly. Furthermore, minor editorial changes are introduced throughout the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/10/2014	06/02/2015	SmPC and PL	In clinical trials, the types of adverse events experienced by patients exposed to supratherapeutic doses were not clinically different from those of patients administered recommended doses of lacosamide. Following doses of 1,200 mg/day, symptoms related to the central nervous system (e.g. dizziness) and the gastrointestinal system (e.g. nausea, vomiting) were observed and resolved with dose adjustments. The highest reported overdose for lacosamide was 12,000 mg taken in conjunction with toxic doses of multiple other antiepileptic drugs. The subject was initially comatose with AV block and then fully recovered without permanent sequelae. In post-marketing, following acute single overdoses ranging between 1,000 mg and 12,000 mg, seizures (generalized tonic-clonic seizures, status epilepticus) and cardiac conduction disorders were observed. Fatal cardiac arrest was reported after an acute overdose of 7,000 mg of lacosamide in a patient with cardiovascular risk factors.
II/0046	Update of section 4.8 of the SmPC in order to include the adverse drug reactions Stevens-Johnson syndrome, toxic epidermal necrolysis and Drug Reaction with Eosinophilia and Systemic Symptoms. The Package Leaflet was updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/04/2014	06/02/2015	SmPC and PL	Cumulatively, since start of marketing of Vimpat, 18 cases of three different severe forms of skin reactions have been identified. Some of these cases occurred in after start of lacosamide treatment or resolved after treatment stopped. Therefore, the CHMP considered that it was not possible to exclude that lacosamide has caused these events and consequently agreed to add these possible side effects to the product information.

IB/0049	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	22/04/2014	n/a		
II/0045	Update of section 4.8 of the SmPC in order to update the safety information by including paresthesia, diarrhea, contusion, and feeling drunk as common adverse drug reactions. The Package Leaflet was updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/03/2014	06/02/2015	SmPC and PL	During the review of data from a study investigating if Vimpat is effective if patients treated with a combination of two or more antiepileptic drugs including Vimpat are converted to Vimpat monotherapy, four new side effects, tingling (paresthesia), diarrhea, bruise, and feeling drunk, were identified in the study and the product information was updated accordingly.
II/0044	Update of section 4.5 of the SmPC in order to update the safety information to inform on the absence of drug-drug-interactions between lacosamide and warfarin. In addition, minor changes were made to the labelling of the solution for infusion. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/02/2014	06/02/2015	SmPC and Labelling	Based on the review of the results from a phase I drug-drug interaction study, the CHMP concluded that lacosamide did not affect the uptake and fate of warfarin in(to) the body nor did it influence the anti-blood clotting effect of warfarin in a clinically meaningful manner. Likewise, the safety profile of lacosamide remained unchanged when administered concomitantly with warfarin.
IA/0047	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	05/02/2014	n/a		
IA/0043/G	This was an application for a group of variations.	18/11/2013	n/a		

	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) A.7 - Administrative change - Deletion of manufacturing sites				
R/0041	Renewal of the marketing authorisation.	30/05/2013	31/07/2013	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 lacosamide when used in the approved indication. The CHMP therefore concluded that the benefit/risk balance of lacosamide as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16-18 years) patients with epilepsy remained favourable and recommended the renewal of the marketing authorisation with unlimited validity.
IA/0042	A.7 - Administrative change - Deletion of manufacturing sites	27/06/2013	n/a		
II/0038/G	This was an application for a group of variations. Addition of a new manufacturer for lacosamide solution for infusion and consequent changes to the manufacturing process. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the	13/12/2012	13/12/2012		

	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 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.3.z - Change in the manufacturing process of the finished product - Other variation B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the currently approved batch size B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
IAIN/0040/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a	12/12/2012	31/07/2013	SmPC, Annex II, Labelling and PL	

	manufacturing site for the FP - Secondary packaging site B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes				
II/0032	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	18/10/2012	22/11/2012	SmPC and PL	
IG/0222	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/11/2012	n/a		
II/0037	Update of Section 4.8 of the SmPC in order to add agranulocytosis as adverse drug reaction.	20/09/2012	24/10/2012	SmPC and PL	This update of the Product Information was based on a request by the CHMP following the assessment of Vimpat

	C.I.3.b - Implementation of change(s) requested 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				PSUR 5, which included several post-marketing reports of cases of impaired white blood cell formation in patients treated with lacosamide. Consequently, the Product Information was updated to include agranulocytosis as an adverse event in section 4.8 of the SmPC to reflect the potential risk of severe forms of lowered number of white blood cells in the blood stream. Due to the limited available data, the frequency could not be determined and was therefore indicated as being unknown. The Package Leaflet was updated in accordance.
IB/0036	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)	31/07/2012	24/10/2012	SmPC	
IA/0035/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.III.2.a.2 - Change of specification(s) of a former non Pharmacopoeial substance to comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material	26/06/2012	n/a		
IB/0034	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)	05/06/2012	24/10/2012	SmPC	
II/0033/G	This was an application for a group of variations.	24/05/2012	24/05/2012		

	Addition of a manufacturing site for the finished product with consequent changes to the manufacturing process. Change in in process controls and limits, and batch size and range. 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 B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site 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.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold 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.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new tests and limits B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test				

	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation				
II/0031	The current type II variation aims at modifying the approved PI for Vimpat in order to align with safety data presented in the 5th Vimpat PSUR. The post marketing event 'hallucination' has been added to the adverse drug reaction table in section 4.8 of the SmPC, and section 4 of the PL 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	19/01/2012	19/03/2012	SmPC and PL	During the post-marketing follow-up for Vimpat, 'hallucination' has been reported as an adverse reaction in 33 cases with temporal relationship observed in 10 cases and a positive dechallenge in 13 cases. As a result, the MAH has added 'hallucination' to the adverse drug reaction table in the SmPC section 4.8 with a footnote that this adverse reaction has been reported post-marketing. The PIL has been updated accordingly. The category of frequency is 'uncommon' (0.3%) based on the results from the pivotal randomised trials.

X/0027	Annex I_2.(c) Change or addition of a new strength/potency	15/12/2011	21/02/2012	SmPC, Annex II, Labelling and PL	Please refer to the Assessment Report: Vimpat-H-863-X-27-AR
A20/0026	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 08 July 2011 the opinion of the CHMP on whether the marketing authorisation of Vimpat should be maintained, varied, suspended or withdrawn in view of a quality issue related to the presence of flake-like precipitates in Vimpat syrup formulation that was identified as lacosamide and had an impact on the effectively administered dose (risk of under or over dosing)	22/09/2011	24/11/2011	SmPC, Labelling and PL	Please refer to the Assessment Report: Vimpat-H-863-A20-26-Assessment Report-Article 20
IB/0029	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	09/11/2011	n/a		
IG/0121	C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	03/11/2011	n/a		
IA/0028/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	16/09/2011	n/a	Annex II and PL	

	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 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 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.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.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.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing 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)				
II/0023/G	This was an application for a group of variations. Addition of an alternative manufacturer for the active	23/06/2011	23/06/2011		

	substance lacosamide. Change to the specification of the immediate packaging for the active substance. Minor change to the manufacturing process of the active substance. B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions B.I.c.2.c - Change in the specification parameters and/or limits of the immediate packaging of the AS - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
IB/0024/G	This was an application for a group of variations. 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 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.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid	22/06/2011	n/a		

	oral dosage form or oral solutions 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.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test				
IA/0025/G	This was an application for a group of variations. 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.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	22/06/2011	n/a		
IB/0021	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 corresponding test method	20/05/2011	n/a		
II/0017/G	This was an application for a group of variations. This was an application for a group of variations. The PI for Vimpat has been amended to align with safety data presented in the 3rd Vimpat PSUR. The post marketing events of suicide attempt and suicidal	17/03/2011	06/05/2011	SmPC, Annex II and PL	Following this group of variations, the PI for Vimpat has been amended to align with safety data presented in the 3rd and 4th PSURs. The post marketing uncommon events of suicide attempt, suicidal ideation, atrial fibrillation, atrial flutter, aggression, agitation, psychotic disorder, angioedema and urticaria, and the common event

	ideation have been added to the adverse drug reaction table in section 4.8 of the SmPC, and the PL has been updated accordingly. Annex IIB has been amended with deletion of the version nr of the DDPS. In addition, the PI for Vimpat has been amended to align with safety data presented in the 4th Vimpat PSUR. Information regarding second-degree or higher atrioventricular (AV) block, atrial fibrillation, and atrial flutter has been added to section 4.4 of the SmPC. The post marketing events of atrial fibrillation, atrial flutter, aggression, agitation, insomnia, psychotic disorder, angioedema and urticaria have been added to the adverse drug reaction table in section 4.8 of the SmPC, and atrial fibrillation and atrial flutter have been added in the description of selected adverse reactions below the table. The PL has been amended accordingly. The PI has been revised to be in line with the new version of the QRD template, and the list of local representatives in the PL has been updated. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				insomnia, have been added to the adverse drug reaction table in section 4.8 of the SmPC. Atrial fibrillation and atrial flutter have been added in the description of selected adverse reactions below the table. Information regarding cardiac rhythm disorders (second-degree or higher atrioventricular block, atrial fibrillation and atrial flutter) has been added to section 4.4 of the SmPC. The PL has been amended accordingly.
IA/0020/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name	06/04/2011	n/a		

	and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites				
IB/0022	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	04/04/2011	n/a		
IB/0019	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	21/03/2011	n/a		
IA/0018	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)	22/02/2011	n/a		
IB/0016	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)	10/01/2011	n/a	SmPC	
II/0012	Update of section 4.8 of the SPC for Vimpat to align with safety data presented in the second and third Vimpat PSURs as well as with the CHMP evaluation of the data pertaining to these PSURs. The Package Leaflet has been updated accordingly.	23/09/2010	25/10/2010	SmPC and PL	Update of the Product Information for Vimpat in line with the CHMP request after the assessment of PSUR 2 and 3. 'Liver function test abnormal', 'drug hypersensitivity' and 'euphoric mood' have been added to section 4.8 as adverse reactions reported in post marketing experience. In

	C.I.3.b - Implementation of change(s) requested 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				addition, information has been added to section 4.8 about 'Laboratory abnormalities', Multiorgan Hypersensitivity Reactions' and 'second and third degree AV block'. The PL has been updated accordingly.
II/0011	Update of the Vimpat SPC sections 4.5 and 5.2 following the results of a recently completed in vitro metabolism study (Study NCD2005). C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	23/09/2010	25/10/2010	SmPC	With this Type II variation, the Vimpat SPC sections 4.5 and 5.2 have been modified following the results of a recently completed in vitro metabolism study (Study NCD2005). The primary objective of Study NCD2005 was to characterize the human hepatic enzymes responsible for lacosamide demethylation which is the major metabolic pathway for lacosamide in humans.
II/0013	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	22/07/2010	06/09/2010	SmPC	To further investigate the interaction of lacosamide with the CRMP-2 protein, the MAH conducted three in vitro binding studies. The results from these additional studies showed that there is no evidence for a specific interaction of lacosamide with CRMP-2 as being part of the mode of action for lacosamide. Based on these new findings, section 5.1 of the SPC has been amended with deletion of the CRMP-2 related mode of action statement.
IA/0014/G	This was an application for a group of variations. B.II.a.3.a.1 - Changes in the composition (excipients) of the finished product - Changes in components of the flavouring or colouring system - Addition , deletion or replacement B.II.a.3.a.1 - Changes in the composition	01/07/2010	n/a	SmPC, Labelling and PL	

	(excipients) of the finished product - Changes in components of the flavouring or colouring system - Addition , deletion or replacement B.II.a.4.a - Change in coating weight of oral dosage forms or change in weight of capsule shells - Solid oral pharmaceutical forms				
II/0008	Update of section 4.8 of the SPC to reflect safety data from PSUR 1 and deriving from post-marketing experience. Update of Summary of Product Characteristics and Package Leaflet	22/04/2010	02/06/2010	SmPC and PL	Rash, bradycardia and AV block have been added to the table in section 4.8 as post marketing events. Additional adverse events have been added to the table in section 4.8, and adverse reactions potentially related to intravenous administration of lacosamide have been added to the Product Information for the lacosamide i.v. formulation only. The PL has been updated accordingly.
IA/0010/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities	18/05/2010	n/a	Annex II and PL	

	C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
II/0009	Fulfillment of FUM 001, extension of shelf-life and change in storage conditions Quality changes	18/03/2010	27/04/2010	SmPC, Labelling and PL	
II/0007	Update of Section 4.5 (Interaction with other medicinal products and other forms of interactions) of the SPC based on the result of a new in vivo drug interaction study with midazolam. The MAH has taken the opportunity to make an editorial change in section 4.6 of the SPC. In addition, minor modifications were introduced in the labelling. Update of Summary of Product Characteristics and Labelling	19/11/2009	21/12/2009	SmPC and Labelling	A new in vivo pharmacokinetic drug interaction study with oral midazolam was submitted in this variation application. This study was a single-site, open-label, non-randomised phase 1 trial, including 36 healthy volunteers. The aim of this study was to investigate the influence of single and repeated administration of lacosamide on the pharmacokinetics of midazolam. Apart from a slight increased Cmax of midazolam after repeated dose administration of lacosamide, no change from baseline in the plasma concentration versus time profile was observed during the co-administration of lacosamide. The results of this drug interaction study with midazolan showed that lacosamide does not affect CYP3A4 in vivo to an extent that is clinically relevant.
II/0006	Change to the manufacturing process for the active substance, i.e, addition of an alternative manufacturing site. Change(s) to the manufacturing process for the active substance	22/10/2009	10/11/2009		

II/0004	Update of the Detailed Description of the Pharmacovigilance System (DDPS) in Module 1.8.1 of the Vimpat Marketing Authorisation to version 5.0 dated 2 June 2009. Annex II has been updated to reflect the new version number of the DDPS. In addition, the labelling was updated with minor linguistic corrections and the local representatives section of the package leaflet was also updated. Changes to QPPV Update of DDPS (Pharmacovigilance)	25/06/2009	24/07/2009	Annex II, Labelling and PL	With this variation the MAH submitted an updated DDPS (version 5.0). After assessing the documentation the CHMP concluded that the submitted DDPS contains all required elements. The Annex II was therefore updated to include the version number of the new DDPS.
II/0001	Update to the sections 4.4 of the Summary of Product Characteristics and 2 of the Package Leaflet following the CHMP assessment of signal of suicidal ideation and behaviour in patients treated with antiepileptics. Update of Summary of Product Characteristics and Package Leaflet	18/12/2008	02/02/2009	SmPC and PL	Due to concerns over the potential risk of suicidal thoughts and behaviour in association with the use of antiepileptics, data available from randomized placebo controlled trials and from the post-marketing phase for this class of medicines was considered by the CHMP. Overall, despite the small number of events seen in the clinical trials and the lack of a statistically significant increased risk of suicidal behaviour, the analysis of randomized placebo controlled trials of antiepileptic drugs did not exclude the possibility of an increased risk. Therefore, the CHMP considered it necessary to update section 4.4 of the SPC and section 2 of the PL with information regarding suicidal ideation and behaviour.
IB/0002	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	14/01/2009	14/01/2009	SmPC, Labelling and PL	
IA/0003	IA_36_ b_Change in shape or dimensions of the	19/12/2008	n/a		

	container/closure - other pharm. forms				