Zebinix

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
PSUSA/1267/ 202104	Periodic Safety Update EU Single assessment - eslicarbazepine acetate	16/12/2021	04/03/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1267/202104.
IB/0083	B.II.d.z - Change in control of the Finished Product - Other variation	08/02/2022	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).

IA/0084	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	24/01/2022	n/a		
IB/0081	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	20/01/2022	n/a		
IA/0082	A.7 - Administrative change - Deletion of manufacturing sites	05/01/2022	n/a		
IA/0080	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	16/12/2021	n/a		
IA/0079	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	01/10/2021	n/a		
IB/0078/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.2.a - Changes in the manufacturing process of	18/08/2021	n/a		

	the AS - Minor change in the manufacturing process of the AS 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) B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - 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.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test				
IB/0076	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	03/05/2021	n/a		

	re-test period/storage period supported by real time data				
N/0075	Update of the Package Leaflet with revised contact details of local representative for Belgium, Luxembourg, the Netherlands, Germany, Hungary, Austria, Czech Republic, France, Ireland, Slovakia, Italy, Denmark, Finland, Iceland, Norway, Sweden and UK. Additionally, the MAH took the opportunity to introduce minor editorial amendments to the local representative entry for Greece. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/01/2021	10/05/2021	PL	
II/0074	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/04/2020	10/05/2021	SmPC and PL	
IAIN/0073/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	04/12/2019	n/a		
PSUSA/1267/ 201810	Periodic Safety Update EU Single assessment - eslicarbazepine acetate	27/06/2019	23/09/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1267/201810.

IB/0072/G	This was an application for a group of variations. 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 B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	20/06/2019	n/a		
IA/0071	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	10/05/2019	n/a		
II/0069	Update of section 4.2 of the SmPC in order to update information related to the switch of tablet and suspension formulation based on the final results from study IA-2093-132, a pharmacokinetic study conducted to address the post-approval commitment: to compare the pharmacokinetic profile of the oral suspension versus the tablets. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/03/2019	06/06/2019	SmPC	The SmPC section 4.2 has been updated as follows: Based on comparative bioavailability data for the tablet and the suspension formulations, switching patients from one formulation to the other can be done.
II/0067	Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data obtained from the open-label extensions (parts II to	31/01/2019	06/06/2019	SmPC	The SmPC section 4.8 and 5.1 have been updated as to include long-term safety data in the paediatric population obtained from open label extensions of the phase III study

	V) of the phase III study BIA-2093-305. The study was assessed in procedure EMA/H/C/988/P46 025. 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				and confirm that it was consistent with the known safety profile of the product with no new findings of concern.
IAIN/0068	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	14/11/2018	n/a		
IA/0066	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/07/2018	n/a		
II/0064	Update of sections 4.4 and 4.8 of the SmPC to add information on urticaria, angioedema and severe cutaneous adverse reactions (SCARS) including Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) as adverse drug reactions with unknown frequency, based on recent post-marketing safety data on Zebinix treatment. 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	17/05/2018	06/06/2019	SmPC and PL	Based on safety data from post-marketing sources (including spontaneous, health authority, and literature reports, respectively) and serious adverse events from interventional and non-interventional clinical trials, there is a causal association between urticaria, angioedema, severe cutaneous adverse reactions (SCARS) including Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) and Zebinix. The Product information has been updated accordingly.

IA/0065/G	This was an application for a group of variations. 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) B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	10/04/2018	n/a		
IB/0063/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.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 C.I.6.z - Change(s) to therapeutic indication(s) - Other variation	28/07/2017	18/09/2017	SmPC, Labelling and PL	
II/0053	Extension of indication for the tablet formulation to	23/03/2017	28/04/2017	SmPC, Annex	For further information, please refer to the scientific

	include the use of Zebinix as monotherapy in the treatment of partial-onset seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy, in addition to the previously authorised indication as adjunctive therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC have been updated. The Package Leaflet was updated in accordance. Furthermore, the product information is being brought in line with the latest QRD template version. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one			II, Labelling and PL	discussion Zebinix EMEA/H/C/000988/II/0053.
IB/0061/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.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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	26/04/2017	n/a		

IB/0062/G	This was an application for a group of variations. B.III.1.a.1 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	20/04/2017	n/a		
IB/0060	B.II.f.1.a.2 - Stability of FP - Reduction of the shelf life of the finished product - After first opening	13/02/2017	28/04/2017	SmPC, Labelling and PL	
IB/0059	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)	04/01/2017	28/04/2017	SmPC	
II/0058	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	15/12/2016	n/a		
X/0050/G	This was an application for a group of variations. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one Annex I_2.(d) Change or addition of a new pharmaceutical form	13/10/2016	08/12/2016	SmPC, Annex II, Labelling and PL	

IA/0057	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/07/2016	n/a		
IB/0056/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.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.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.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	13/05/2016	n/a		
PSUSA/1267/201510	Periodic Safety Update EU Single assessment - eslicarbazepine acetate	13/05/2016	n/a		PRAC Recommendation - maintenance
IA/0054/G	This was an application for a group of variations.	04/05/2016	n/a		

	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.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.III.2.a.2 - 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 - Excipient/AS starting material B.III.2.a.2 - 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 - Excipient/AS starting material				
IB/0055	B.I.c.2.z - Change in the specification parameters and/or limits of the immediate packaging of the AS - Other variation	29/04/2016	n/a		
N/0052	Update of the package leaflet with revised contact details of the local representative for Spain. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/04/2016	08/12/2016	PL	
PSUSA/1267/201410	Periodic Safety Update EU Single assessment - eslicarbazepine acetate	21/05/2015	28/07/2015	SmPC and PL	Please refer to Zebinix PSUSA-1267-201410 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IAIN/0049/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of	01/07/2015	n/a		

	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 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.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				
IA/0048	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	07/04/2015	n/a		
IB/0047/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.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	27/03/2015	n/a		

	Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
II/0044	Update of sections 4.2 and 5.1 of the SmPC with information from the concluded safety and efficacy study BIA-2093-401 in the elderly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/09/2014	16/03/2015	SmPC	The safety and efficacy of eslicarbazepine acetate as adjunctive therapy for partial seizures in elderly patients were evaluated in one non-controlled study, with a duration of 26 weeks, in 72 elderly (aged ≥ 65 years). The data shows that the incidence of treatment emergent adverse events in this population (65.3 %) is similar to the general population enrolled in the double-blind epilepsy studies (66.8%).The most frequent individual treatment emergent adverse events were dizziness (12.5% of subjects), somnolence (9.7%), fatigue, convulsion and hyponatraemia (8.3%, each), nasopharyngitis (6.9%) and upper respiratory tract infection (5.6%). A total of 50 of the 72 subjects starting the study completed the 26-week treatment period that corresponds to a retention rate of 69.4%. No dose adjustment is needed in the elderly population

					provided that the renal function is not disturbed.
II/0041	The MAH submitted the final report of study BIA-2093-208 in children aged 6 to less than 16 years investigating the safety and efficacy of eslicarbazepine acetate in refractory partial onset seizures, including effect on cognitive function. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	22/05/2014	n/a		In this variation the company provided data from a recently completed study in children between 6-16 years of age with partial onset seizures refractory to treatment. The provided data did not change the product information of Zebinix.
IA/0045	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	21/05/2014	n/a		
PSUV/0043	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
II/0035	Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information based on the results from a newly completed phase III study in adult patients with refractory partial onset seizures as well as a an updated integrated safety analysis of available placebo-controlled clinical trials and other cumulative safety data. The Package Leaflet was updated accordingly. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	20/03/2014	16/03/2015	SmPC, Annex II and PL	Following completion of the placebo-controlled part of a new study with Zebinix, an updated integrated analysis of all available placebo-controlled clinical safety data was performed. The review of these data in conjunction with cumulative safety information from open label studies, post-marketing reports and the known safety profile of other antiepileptic drugs of the same class resulted in the need to adjust the safety information. Several terms for adverse drug reactions were combined or deleted, frequencies were corrected and new terms were added. One new important potential risk of bone disorders was identified, which may be a class effect. Furthermore, one

					case of severe rash has been reported.
IB/0042/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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	29/01/2014	n/a		
R/0040	Renewal of the marketing authorisation.	21/11/2013	22/01/2014	SmPC, Annex II and PL	Based on the review of the cumulative quality, efficacy and safety data 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 Zebinix when used in the approved indication. The CHMP therefore concluded that the benefit/risk balance of Zebinix as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation remained favourable and recommended the renewal of the marketing authorisation with unlimited validity.
IA/0039	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/07/2013	n/a		
IB/0037	B.I.b.2.e - Change in test procedure for AS or	22/04/2013	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
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)	15/04/2013	22/01/2014	SmPC	
IA/0038/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 currently approved batch size 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	09/04/2013	n/a		
IB/0033	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	30/11/2012	n/a		
IAIN/0034/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	16/11/2012	n/a		

	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 oral dosage form or oral solutions				
IB/0032/G	This was an application for a group of variations. 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 C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/11/2012	14/01/2013	SmPC, Labelling and PL	C.I.3.a - Update of Section 4.4 of the SmPC to implement revised wording in relation to risk of hypersensitivity reactions potentially associated with HLA-A*3101 allele in Europeans and Japanese and recommendations on testing for HLA-B*1502 allele in some Asian populations as requested by the CHMP in July 2012. C.I.z – Update of Section 4.2 of the SmPC to implement dose recommendations for patients with renal insufficiency to use an optional initial dose of 200 mg once daily following the approval of the new 200mg tablet strength.
IB/0031/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.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.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	27/09/2012	n/a		

WS/0258	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Section 4.5 of the SmPC is updated in order to add information on the interaction with rosuvastatin. The Package Leaflet is updated accordingly. In addition, the list of local representatives in the Package Leaflet of Zebinix is updated. Furthermore, the PI is being brought in line with the latest QRD template version 8. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/06/2012	23/08/2012	SmPC, Annex II, Labelling and PL	This variation updated the Product Information of Exalief and Zebinix to reflect data from a clinical study which showed that concomitant treatment with rosuvastatin and eslicarbacepine acetate reduces rosuvastatin plasma concentration and available amount.
X/0024	Annex I_2.(c) Change or addition of a new strength/potency	21/06/2012	23/08/2012	SmPC, Labelling and PL	
IB/0030	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	20/06/2012	23/08/2012	SmPC	Implementation of agreed wording in sections 5.3 and 6.6 of the SmPC following the assessment of FU2 001.3 in order to inform about the environmental risk of eslicarbazepine acetate as well as provide advice on disposal.
IB/0029/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	21/05/2012	n/a		

	batch control/testing takes place 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				
IB/0027	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)	10/02/2012	23/08/2012	SmPC	
WS/0120	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To add an alternative manufacturer of the active substance (eslicarbazepine acetate). 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	15/12/2011	15/12/2011		
WS/0162	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 SPC to add a number of adverse reactions resulting from CHMP assessment of an additional pooled analysis of phase III data. The PL has been updated accordingly. In addition, a	22/09/2011	10/11/2011	SmPC and PL	After CHMP assessment of the results obtained on an additional pooled analysis of the phase III data for eslicarbazepine acetate, the MAH has submitted a type II variation to add the adverse events 'irritability', 'chest pain' and 'urinary tract infection' to section 4.8 of the SPC as 'uncommon' events under the respective System Organ Class.

	cross-reference has been corrected in section 4.6 of the SmPC, and the contact details for the local representative in The Netherlands have 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				
IA/0023/G	This was an application for a group of variations. 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 oral dosage form or oral solutions B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	27/10/2011	n/a		
IA/0022/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.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	18/10/2011	n/a		
IA/0021/G	This was an application for a group of variations.	13/04/2011	n/a	Annex II	

	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV 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/0018/G	This was an application for a group of variations. 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	21/10/2010	29/11/2010	SmPC and PL	Eslicarbazepine acetate is an antiepileptic drug which is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation. At the time of the approval, the CHMP requested the MAH to investigate the possible drug-drug interaction with carbamazepine as a follow-up measure. In addition, the CHMP requested the investigation of the inducing effect of eslicarbazepine acetate on CYP3A4 in humans as a follow-up measure. In a drug-drug interaction study with carbamazepine, it was shown that concomitant administration of eslicarbazepine acetate 800 mg once daily and carbamazepine 400 mg twice daily resulted in an average decrease of approximately 30 % in exposure to the active metabolite eslicarbazepine most likely caused by an increase in metabolism. The dose of eslicarbazepine acetate may therefore need to be increased when used concomitantly with carbamazepine. Concomitant intake of eslicarbazepine acetate did not alter the pharmacokinetic profile of carbamazepine or its metabolite carbamazepine-epoxide. A study to examine the induction of CYP3A4 by

					eslicarbazepine acetate showed an average decrease of approximately 50 % in systemic exposure to simvastatin when co-administered with eslicarbazepine acetate 800 mg once daily. An increase of the simvastatin dose may therefore be required when used concomitantly with eslicarbazepine acetate. Section 4.5 of the SPC and section 2 of the PL have been updated with the new information, and the PI has been revised according to the current QRD template.
IA/0020/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.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.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	26/11/2010	n/a		

	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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				
IB/0019	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)	28/10/2010	n/a	SmPC	
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/12/2009	n/a	PL	
IB/0016	IB_17_a_Change in re-test period of the active substance	19/10/2009	n/a		
IA/0015	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	29/09/2009	n/a		
IB/0007	IB_14_b_Change in manuf. of active substance without Ph. Eur. certificate - new manufacturer	05/06/2009	n/a		
IB/0006	IB_14_a_Change in manuf. of active substance	05/06/2009	n/a		

	without Ph. Eur. certificate - change in manuf. site				
IB/0005	IB_14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	05/06/2009	n/a		
IB/0004	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	05/06/2009	n/a		
IB/0003	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	05/06/2009	n/a		
IA/0014	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	18/05/2009	n/a		
IA/0013	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	18/05/2009	n/a	Annex II and PL	
IA/0012	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	18/05/2009	n/a		
IA/0011	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	18/05/2009	n/a		
IA/0010	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	18/05/2009	n/a		
IA/0009	IA_32_b_Change in batch size of the finished product - downscaling down to 10-fold	18/05/2009	n/a		

IA/0008	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	18/05/2009	n/a		
IA/0002	IA_13_a_Change in test proc. for active substance - minor change	18/05/2009	n/a		
IA/0001	IA_13_a_Change in test proc. for active substance - minor change	18/05/2009	n/a		