EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Exalief

Procedural steps taken and scientific information after the authorisation

No	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IB/0025	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	n/a	SPC	
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	n/a		
IA/0021/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	27/10/2011	n/a		

[1] Notifications are issued for type I variations (unless part of a group or a worksharing application). Opinions are issued for all other procedures.
[2] No Commission Decision is issued for type IA and type IB variations or for type II variations and annual re-assessments that do not affect the annexes.
[3] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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No	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
	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				
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 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	22/09/2011	27/10/2011	SPC, 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.
IA/0020/G	This was an application for a group of variations. 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	13/04/2011	n/a	Annex II	

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II/0017/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	SPC, Annex II, 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/0019/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,	26/11/2010	n/a		

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	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, 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.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/0018	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	SPC	
IB/0016	17_a_Change in re-test period of the active substance	19/10/2009	n/a		
IA/0015	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/0004	13_b_Change in test proc. for active substance - other changes (replacement/addition)	05/06/2009	n/a		
IB/0007	14_b_Change in manuf. of active substance	05/06/2009	n/a		

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	without Ph. Eur. certificate - new manufacturer				
IB/0006	14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	05/06/2009	n/a		
IB/0005	14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	05/06/2009	n/a		
IB/0003	13_b_Change in test proc. for active substance - other changes (replacement/addition)	05/06/2009	n/a		
IA/0001	13_a_Change in test proc. for active substance - minor change	14/05/2009	n/a		
IA/0002	13_a_Change in test proc. for active substance - minor change	14/05/2009	n/a		
IA/0008	38_a_Change in test procedure of finished product - minor change to approved test procedure	14/05/2009	n/a		
IA/0009	32_b_Change in batch size of the finished product - downscaling down to 10-fold	14/05/2009	n/a		
IA/0014	07_a_Replacement/add. of manufacturing site: Secondary packaging site, 07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	14/05/2009	n/a		
IA/0013	08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	14/05/2009	n/a	Annex II, PL	
IA/0010	38_a_Change in test procedure of finished product - minor change to approved test procedure	14/05/2009	n/a		
IA/0011	38_a_Change in test procedure of finished product - minor change to approved test procedure	14/05/2009	n/a		

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IA/0012	38_a_Change in test procedure of finished product - minor change to approved test procedure	14/05/2009	n/a		