Rivastigmine Actavis

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/0032	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	07/02/2024		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).

IG/1612	A.1 - Administrative change - Change in the name and/or address of the MAH	31/05/2023		SmPC, Labelling and PL	
IAIN/0030	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	09/05/2022	05/05/2023	Annex II and PL	
IA/0029/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	04/04/2022	n/a		
IB/0028	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)	15/03/2022	07/06/2022	SmPC, Labelling and	

				PL	
IA/0027	A.7 - Administrative change - Deletion of manufacturing sites	09/04/2021	07/06/2022	Annex II and PL	
IA/0026	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	08/07/2020	n/a		
IB/0025	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	02/07/2019	n/a		
IA/0024/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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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	21/06/2019	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation				
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/04/2018	07/06/2022	PL	
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/07/2017	07/06/2022	Labelling and PL	

IB/0020/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 importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	06/01/2017	n/a		
IA/0021	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	05/01/2017	n/a		
IAIN/0019/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.c.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 -	25/04/2016	16/02/2017	Annex II and PL	

	Not including batch control/testing 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				
IAIN/0018/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.c.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	17/02/2016	16/02/2017	Annex II and PL	
R/0016	Renewal of the marketing authorisation.	17/12/2015	15/02/2016	Annex II and Labelling	
IB/0017	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	07/12/2015	15/02/2016	SmPC and PL	

IB/0015/G	This was an application for a group of variations. C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO	04/09/2015	15/02/2016	SmPC, Annex II, Labelling and PL	

	new additional data is required to be submitted by the MAH				
IB/0013/G	This was an application for a group of variations. C.I.7.a - Deletion of - a pharmaceutical form C.I.7.b - Deletion of - a strength	03/06/2015	15/02/2016	SmPC, Annex II, Labelling and PL	
IB/0014/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.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	22/05/2015	n/a		
IAIN/0012/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	26/03/2015	n/a		

N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/08/2014	15/02/2016	PL	
N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/01/2014	15/02/2016	PL	Update of details for local representatives in Annex IIIB.
N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/08/2013	15/02/2016	PL	Exchanging a graphic in the product information leaflet.
II/0008	To add an alternative manufacturer of the active substance (rivastigmine hydrogen tartrate) for manufacture of Rivastigmine capsules. B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is supported by an ASMF	27/06/2013	n/a		
X/0005	Line extension (addition of new pharmaceutical form /new route of administration). Transdermal Patches of 4.6 mg/24 hours and 9.5 mg/24 hours. Annex I_2.(d) Change or addition of a new pharmaceutical form	21/02/2013	17/04/2013	SmPC, Annex II, Labelling and PL	The MAH applied for the addition of a new pharmaceutical form / new route of administration. Transdermal patches have been developed as generic products to Exelon transdermal patches (4.6 mg/24 hours and 9.5 mg/24 hours). The composition per unit area is identical for both strengths. The manufacturing process has been described and critical steps identified. Information on development, manufacture and control of this new pharmaceutical form has been presented. The product development has been described and several in vitro and in vivo proofs of concept clinical studies have been performed before the final composition was chosen and tested in a bioequivalence study. The in

					vitro method chosen for the control of the drug substance prove similarity between the two strengths. Data has been provided showing that the method is discriminatory. The applicant has also presented data to ensure adhesion equivalence between the two dosage strengths.
IB/0007	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data are submitted by the MAH	11/07/2012	n/a	SmPC and PL	Update of SmPC and PL in line with updates of the originator's product Exelon/Prometax (WS-132) adopted on 16 March 2012. Update of section 4.8 of the SmPC to reflect the safety findings of the open-label safety study in patients with Parkinson's disease dementia. Additionally, sections 4.3 and 4.4 were updated with information on skin application site reactions and skin hypersensitivity, recommendations on formulation switching and treatment discontinuation. The Package Leaflet was updated in accordance. Minor editorial changes were introduced throughout the Product Information.
IB/0006/G	This was an application for a group of variations. C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data are submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data are submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a	12/03/2012	25/05/2012	SmPC and PL	To update the SmPC and PL in line with updates of the originator's product Exelon/Prometax introduced in the work sharing procedures WS-119 and WS-121-G, which were adopted by the CHMP on 14 April 2011. The EMA variation request EMA/360627/2011 was dated 10 January 2012. C.I.2a) WS-119 included the following updates: Update of sections 4.3 and 4.4 of Exelon/Prometax oral formulations SmPC to change the contraindication for patients with severe hepatic impairment into a warning, in accordance with Exelon/Prometax transdermal patch SmPC. Section 4.4 of the SmPC for the oral formulations is also revised to reflect that patients with clinically significant

	generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data are submitted by the MAH				renal or hepatic impairment might experience more adverse reactions. Section 4.2 is amended accordingly. In addition, minor linguistic amendments have been introduced in the SmPC in line with the reference medicinal product. The Package Leaflet has been amended to reflect those changes. Finally, the Package Leaflet of all Rivastigmine Actavis presentations is revised based on the results of a Exelon/Prometax user testing (FUM 026). C.I.2a) WS-121-G included the following updates: Following a request from the CHMP (PSUR 18) and a safety review analysis from the MAH, section 4.8 of the SmPC has been amended to include new adverse reactions: dehydration, hepatitis, aggression, restlessness and sick sinus syndromes. In addition, anxiety has been included in section 4.8 of the Rivastigmine Actavis SmPCs in line with the reference medicinal product. The whole section 4.8 has been revised according to the current MedDRA terminology in line with the reference medicinal product. Section 4.4 of the SmPC for all formulations has also been amended to include that gastrointestinal disorders may occur in patients treated with rivastigmine. The Package Leaflet has been amended to reflect those changes. C.I.2a) WS-121-G included additional updates: Finally, section 4.4 of the oral formulations SmPC has been revised to include a warning for patients with low body weight. The Package Leaflet has been amended to reflect those changes. Additionally, contact information for Czech Republic and

					Cyprus has been updated in sections 6 of the Package Leaflets.
IB/0004	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	12/01/2012	n/a		
IB/0003	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	12/01/2012	n/a		
IB/0001/G	This was an application for a group of variations. B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings	16/11/2011	25/05/2012	SmPC, Labelling and PL	