Prometax

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
WS/2441/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.b.3.z - Change in the manufacturing process of	25/05/2023	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).

	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 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.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				
WS/2442	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.4 and 4.5 of the SmPC in order to strengthen the existing warning on QT prolongation, based on post-marketing data and literature; the Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/04/2023		SmPC and PL	For more information, please refer to the Summary of Product Characteristics and the Package Leaflet.
WS/2378	This was an application for a variation following a	12/01/2023	n/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				
IG/1550/G	This was an application for a group of variations. B.II.e.1.b.3 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Deletion of an immediate packaging container without a complete deletion of a strength or pharmaceutical form A.7 - Administrative change - Deletion of manufacturing sites	14/11/2022		SmPC, Labelling and PL	
N/0140	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/08/2022		PL	
IG/1482	A.7 - Administrative change - Deletion of manufacturing sites	01/02/2022	n/a		
N/0138	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/10/2021	18/11/2021	PL	
IG/1433	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	24/08/2021	n/a		

IG/1432/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.e.1.b.3 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Deletion of an immediate packaging container without a complete deletion of a strength or pharmaceutical form 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	20/08/2021	n/a		
IG/1382/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.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.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer	10/05/2021	18/11/2021	Annex II and PL	

	responsible for importation and/or batch release - Not including batch control/testing 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)				
WS/2021/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.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.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.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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	25/03/2021	n/a		

N/0134	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/03/2021	18/11/2021	PL	
IG/1324/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.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.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	22/12/2020	n/a		
IG/1323/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.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	22/12/2020	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
WS/1955	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/11/2020	18/11/2021	SmPC, Annex II, Labelling and PL	
WS/1773	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Based on the review of the submitted data, this application regarding the following change: Variation requested Type Annexes affected C.I.11.b 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 Type II None Submission of an updated RMP v 10.0 to reflect the results of the Drug Utilisation Study CENA713D2409 (submitted and assessed in variation WS-1557, opinion adopted in July 2019) and to reassess all important risks in accordance of GVP revision 2. In	17/04/2020	n/a		

	addition, as requested by the PRAC following the assessment of the PSUSA/00002654/201901, some safety concerns have been removed. 1 is recommended for approval. The requested worksharing procedure leads to amendments to the Risk Management Plan (RMP). 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				
IG/1219/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	10/04/2020	16/10/2020	Annex II and PL	
IG/1189/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	20/12/2019	n/a		

	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.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.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.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.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.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.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.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)				
IG/1147/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	03/10/2019	16/10/2020	SmPC and Labelling	

	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 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 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 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 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 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				
WS/1645	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.e.1.z - Change in immediate packaging of the finished product - Other variation	03/10/2019	16/10/2020	SmPC and Labelling	

WS/1676/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.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.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.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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.2.a.1 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of	26/09/2019	n/a		

	a Member State - AS				
PSUSA/2654/201901	Periodic Safety Update EU Single assessment - rivastigmine	05/09/2019	n/a		PRAC Recommendation - maintenance
WS/1557	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	11/07/2019	n/a		
IG/1089/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.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	26/04/2019	n/a		
N/0120	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/10/2018	16/10/2020	PL	
IG/0956/G	This was an application for a group of variations.	12/07/2018	n/a		

	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.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				
T/0118	Transfer of Marketing Authorisation	20/03/2018	08/05/2018	SmPC, Labelling and PL	
WS/1321	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/01/2018	08/05/2018	SmPC, Annex II, Labelling and PL	
WS/1293	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	11/01/2018	n/a		

IG/0883	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	21/12/2017	n/a		
WS/1206/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. A.7 - Administrative change - Deletion of manufacturing sites 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.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 - 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 - Changes to quality control testing arrangements for	19/10/2017	n/a		

	the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.g - 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 not supported by an ASMF and requires significant update to the relevant AS section in the dossier 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.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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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				
IG/0729	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	20/09/2016	n/a		
PSUSA/2654/ 201601	Periodic Safety Update EU Single assessment - rivastigmine	02/09/2016	n/a		PRAC Recommendation - maintenance

WS/0946/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.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of	07/07/2016	n/a		

	an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation				
WS/0911/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.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation 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 B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	02/06/2016	n/a		

	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification 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 test(s) and limits B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
PSUSA/2654/201501	Periodic Safety Update EU Single assessment - rivastigmine	24/09/2015	19/11/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2654/201501.
WS/0743	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.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	24/09/2015		Annex II	
N/0109	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/07/2015	19/11/2015	PL	
IG/0589/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	24/07/2015	n/a		

	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				
IG/0564	A.1 - Administrative change - Change in the name and/or address of the MAH	08/05/2015	19/11/2015	SmPC, Labelling and PL	
WS/0621	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.5 and 5.2 of the SmPC in order to add information on drug-drug interactions based on study R1100543, internal database and literature data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 9.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/03/2015	19/11/2015	SmPC, Annex II and PL	In this variation the MAH updated the information on drug-drug interactions of rivastigmine indicating that caution is warranted when Exelon/Prometax are given at the same time as beta-blockers, other bradycardiac agents and some arrhythmogenic medicines, i.e. those inducing Torsades de pointes.
WS/0623	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC section 4.8 based on safety data from studies (D2344, D1301) in the Asian population. Furthermore, sections 4.2 and 4.4 of the	22/01/2015	19/11/2015	SmPC and PL	The MAH proposed updates to the product information following the analysis of data from two studies (D2344, D1301) in Asian patients. Consequently, information that some application site adverse reactions occurred at higher levels in those patients has been added to the section 4.8 of the patch formulation. Additionally, dosing instructions and related warnings for re-initiation of rivastigmine as well

	SmPC are updated in order to harmonise the dosing instructions and related warnings for re-initiation of rivastigmine capsule and oral solution with the dosing instructions and warnings for the patch. 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				as information on side effects have ben harmonised across the product information.
WS/0622	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 4.6 of the SmPC to align it with the Company Core Data Sheet (CCDS) and section 5.3 of the SmPC in order to reflect information from concluded mutagenicity study (Study 1070378) and updated CCDS. Furthermore, editorial changes have been introduced in the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/01/2015	19/11/2015	SmPC	The MAH submitted non-clinical data on cardiovascular safety (Study 1070345), mutagenicity (Study 1070378), and metabolism in human liver microsomes (Study 1100543) which confirmed the known safety and PK profile of rivastigmine and its main metabolite NAP226-90. The Product Information has been revised and updated accordingly.
WS/0625	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC sections 4.2, 4.4 and 5.2 for the transdermal patch formulation with information	18/12/2014	19/11/2015	SmPC	In this WS procedure the MAH updated the product information with information related to special populations, i.e. hepatically and renally impaired patients in order to align the wording of all formulations and to reflect the results of pharmacokinetic analyses of existing data.

	related to special populations, i.e. hepatically and renally impaired patients. Furthermore, the MAH took the opportunity to harmonise wording pertinent to hepatic and renal impairment in SmPC sections 4.2 and 4.4 for the oral formulations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
WS/0624	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 of the transdermal patch formulation with preferred term 'tremor' in AD patients with frequency 'not known'; update of section 4.9 of the SmPC with cholinergic and nicotinic symptoms of overdose and of sections 4.4 and 4.8 with preferred terms 'Parkinson's disease worsening' and 'allergic dermatitis disseminated' for all formulations. The updates are based on post-marketing data. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/12/2014	19/11/2015	SmPC	The Summary of product characteristics of rivastigmine has been revised in order to include a side effect 'tremor in AD patients' with frequency not known to section 4.8 'Undesirable effects' for the transdermal patch formulation. Furthermore, the section 4.9 'Overdose' has been updated to reflect that the signs and symptoms of rivastigmine overdose are dose dependent and that the overdose may show different clinical features based on the dose taken.
PSUSA/2654/ 201401	Periodic Safety Update EU Single assessment - rivastigmine	11/09/2014	n/a		PRAC Recommendation - maintenance

IG/0443	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)	20/08/2014	n/a		
WS/0549/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. - To tighten the limits of known degradation products. - To tighten the limists for unspecified identified impurity. - To tighten the limits of total degradation products. - To tighten the limits for assay. - To add the test for loss on drying. - To delete additional appearance specifications. - To delete test disintegration time. - To delete test mass of content. - To replace uniformity content by uniformity of dosage units. - To replace microbial limit test by microbial enumeration test in accordance with the harmonized pharmacopeia. - Minor change the test procedure of identity. - To replace the test procedure for dissolution. - To replace the test procedure for identity. - To replace the test procedure for degradatiuon products. - To replace the test procedure for assay.	25/04/2014	n/a		

	- To replace the test procedure for determination of content uniformity. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - 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 B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - 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 B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur.				

	2.9.5 or Ph. Eur. 2.9.6 B.II.d.1.h - Change in the specification parameters and/or limits of the finished product - Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
WS/0502/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. This submission provides the following changes for	20/02/2014	n/a		

	rivastigmine hydrogen tartrate used to manufacture oral solution and capsules: To delete a quality control testing site. To add a manufacturing site of the active substance To add a manufacturing site of an intermediate of the active substance. To add a quality control site of the active substance. To add a quality control testing site. To change the manufacturing process of the active substance. To change the manufacturing process of the active substance. To change the manufacturing process of the active substance. To change the manufacturing process of the active substance. To change the raw material specification of the active substance. To change the raw material specification of the active substance. To change the raw material specification of the active substance. To change the raw material specification of the active substance. To change the raw material specification of the active substance. To change the raw material specification of the active substance. To add an specification and test for a reagent. To add the specification and test for a reagent. To add the specification and test a reagent. To add the specification and test for an starting				

	material. To add the specification and test for an starting material. To delete the specification and test for a raw material of the active substance. To delete the specification and test for raw material of the active substance. To delete the specification and test for raw material of the active substance. To add an alternate test method for a reagent. To add an alternate test method for a reagent. A.7 - Administrative change - Deletion of manufacturing sites 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.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.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 - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place 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.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 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.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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - 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.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 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.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.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.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.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
IG/0384	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	27/11/2013	n/a		
IG/0367/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.c - Change in test procedure for AS or starting material/reagent/intermediate - Other	30/10/2013	n/a		

	changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
IG/0370	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	29/10/2013	n/a		
IAIN/0091	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	16/10/2013	07/11/2014	SmPC and PL	
N/0090	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/09/2013	07/11/2014	PL	
IG/0334/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.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a	07/08/2013	n/a		

	manufacturing site for the FP - Secondary packaging site				
IG/0333/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.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site A.7 - Administrative change - Deletion of manufacturing sites 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	07/08/2013	n/a		
IG/0335/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	31/07/2013	n/a		

	site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
WS/0376/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. 1) To add an alternate of the manufacturing site of the active substance. 2) To change in the specification parameters for some reagents reagents 3) To add an alternate manufacturing site ofan intermediate used in the manufacturing of the active substance. 4) To add an specificatication for a reagent used in the manufacturing process of the active substance. 5) To remove a test method from all relevant raw material specifications. 6) To add a new primary quality control site for the active substance. To take the opportunity to amend some editorial errors in Module 3	25/07/2013	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 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.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.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.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.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				
WS/0402/G	This was an application for a group of variations following a worksharing procedure according to	27/06/2013	n/a		

	Article 20 of Commission Regulation (EC) No 1234/2008. This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. -To tighten specification limits for specified impurities. -To change specifications for microbiological testing as a result of the implementation of the internationally harmonised pharmacopoeial monograph for microbial purity of non-sterile materials by adopting Microbial Enumeration Test Method (MET). -To change the test procedure for the assessment of the appearance of the solution to reflect Ph. Eur. 2.2.1 and 2.2.2. -To replace the test procedure for identity, assay, degradation product of the AS and the assay of preservative by HPLC. -To tighten specification limits for unspecified degradation products. -To add a second test for the Identity of the preservative.				

	-To add a second test for the Identity for the AS. -To report pH value test procedure in a more detailed way. -To update Microbiological Limit Test (MLT) with Microbial Enumeration Test (MET) in order to comply with the Ph. Eur. 2.6.12and to update the micro-organism Escherichia Coli test in order to comply with Ph. Eur 2.6.13. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with				

	its corresponding test method 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				
IG/0296/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new or updated 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.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	24/04/2013	n/a		
X/0078/G	This was an application for a group of variations. Annex I_2.(c) Change or addition of a new strength/potency C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	15/11/2012	14/01/2013	SmPC, Annex II, Labelling and PL	Please refer to scientific summary Prometax-H-255-X-78-G-AR.
IG/0248	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/12/2012	n/a		
IG/0209/G	This was an application for a group of variations.	17/08/2012	n/a		

	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.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				
WS/0222/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.e.1.z - Change in immediate packaging of the finished product - Other variation B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation B.II.e.1.z - Change in immediate packaging of the finished product - Other variation	21/06/2012	n/a		
WS/0132/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. 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	15/03/2012	20/04/2012	SmPC, Annex II and PL	In this variation the MAH updated the product information with new safety data based on the results of a study conducted in patients with dementia due to Parkinson's disease. At the same time the MAH updated the contraindications and warnings on skin reactions that may occur during the treatment with Exelon/Prometax capsules, oral solution and patches.

	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. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
WS/0194	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To use the following intermediate product results for release of the finished product (transdermal patch): identification (TLC), degradation products (HPLC), assay (HPLC), dissolution (HPLC), assay and uniformity of dosage unit (HPLC). The MAH also took the oportunity to update the quality documentation with updated validation data for the HPLC methods used for related substances determination and dissolution testing and introduced some minor changes that were requested during the assessment of the original submission. B.II.d.3 - Variations related to the introduction of real-time release or parametric release in the manufacture of the finished product	15/03/2012	15/03/2012		
IG/0148/G	This was an application for a group of variations.	22/02/2012	n/a		

	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.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				
WS/0157/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. Change in the manufacturing process, test procedure and specification parameters of the active substance. 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 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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	15/12/2011	15/12/2011		

	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.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)				
WS/0178	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 and relevant section of the PL to include "elevated liver function tests" to the 5 cm2 and 10 cm2 patch as requested by CHMP during evaluation of PSUR 19. 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	20/10/2011	07/12/2011	SmPC and PL	As already reflected in the capsules and oral formulations for Exelon and Prometax the PI has been amended to include elevated liver function test as possible adverse reaction to the patch formulations. This application was submitted following a worksharing procedure.
IG/0113/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	11/11/2011	n/a		

	B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer				
IG/0075/G	This was an application for a group of variations. 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) A.7 - Administrative change - Deletion of manufacturing sites	16/07/2011	n/a	Annex II and PL	
IG/0088/G	This was an application for a group of variations. 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.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	11/07/2011	n/a		
WS/0121/G	This was an application for a group of variations following a worksharing procedure according to	14/04/2011	23/05/2011	SmPC and PL	Based on a review of the safety data for rivastigmine, new sides effects have been added in rivastigmine Summary of

	Article 20 of Commission Regulation (EC) No 1234/2008. This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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 that was already listed in the transdermal patch SmPC has been included in section 4.8 of the oral formulation SmPCs. The whole section 4.8 has been revised according to the current MedDRA terminology. Section 4.4 of the SmPC for all formulations has also been amended to include that gastrointestinal disorders may occur when in patients treated with rivastigmine. 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. 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				Product Characteristics (SmPC) with the frequency unknown: "dehydration", "hepatitis", "aggression", "restlessness" and "sick sinus syndromes". In addition, the side effect "anxiety" that was already listed in the transdermal patch formulation SmPC has been added in the SmPC for the oral formulations. New warnings for patients with low body weight and patients who experience nausea, vomiting and diarrhoea have also been added in the SmPC. The Package Leaflet has been amended to reflect those changes.

	MAH C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
WS/0119	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. This application was submitted following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008: 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 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. Finally, the Package Leaflet of all Exelon/Prometax presentations is revised based on the results of a user testing (FUM 026) and to reflect changes in the details of local representatives. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-	14/04/2011	23/05/2011	SmPC and PL	The following warning has been added in section 4.4 of the oral solutions SmPCs: Special populations Patients with clinically significant renal or hepatic impairment might experience more adverse reactions (see sections 4.2 and 5.2). Patients with severe hepatic impairment have not been studied. Therefore, if Exelon is used in this patient population close monitoring is necessary. Section 4.2 of the oral formulations SmPCs has also been revised to now include the following: No dose adjustment is necessary for patients with mild to moderate renal or hepatic impairment. However, due to increased exposure in these populations, dosing recommendations to titrate according to individual tolerability should be closely followed as patients with clinically significant renal or hepatic impairment might experience more adverse reactions.

	clinical, clinical or pharmacovigilance data				
IG/0065		17/05/2011	n/a		
IG/0032/G	This was an application for a group of variations. To update the Detailed Description of the Pharmacovigilance System (DDPS) to version 9.0, to include: - a change in the deputy of the Qualified Person for Pharmacovigilance (QPPV); - a change in the major contractual arrangements. - administrative changes not impacting the operation of the pharmacovigilance system. Annex II.B has also been updated with the latest wording as per October 2010 CHMP procedural announcement. 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.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.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	21/12/2010	n/a	Annex II	

WS/0036/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.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 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.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	16/12/2010	16/12/2010		
WS/0032	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	16/12/2010	16/12/2010		

	Change in the manufacturing process of the patches. B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation				
IG/0025/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new or updated 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 or updated 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.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	20/10/2010	n/a		
WS/0031	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To add a new immediate packaging for the active substance B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile)	23/09/2010	23/09/2010		
II/0058	Update of the Summary of Product Characteristics and Package Leaflet on a number of undesirable side	18/03/2010	29/04/2010	SmPC, Annex II and PL	Following the assessment of PSUR 16 the MAH was requested to update the possible side effects section of the

	effects reported post-marketing and update of the overdose section of the SPC for the patch formulation regarding misuse and dosing errors. Update of Summary of Product Characteristics and Package Leaflet				Product Information with additional side effects which have been reported post-marketing with Prometax transdermal patches: High blood pressure, application site allergic reaction, itching, rash, skin reddening, itchy rash, blisters, skin inflammation, fast heart beat, irregular heart beat, severe upper stomach pain, fall, convulsion, worsening of Parkinson disease (tremor, stiffness, shuffling) and hallucinations. Some of these events had already been reported with the oral formulations (Prometax capsules and oral solution). For all formulations, the product information was updated with information on generalised skin reactions. The Product information was also been updated to raise awareness regarding misuse and dosing errors with the patch formulation which could expose patients to an excessive amount of this medicine. In addition, the MAH took the opportunity to correct minor linguistic errors and to update all annexes in all languages to be inline with the current QRD requirements. The MAH also submitted version 3 of the Risk Management Plan (RMP).
II/0059	Update of the Detailed Description of the Pharmacovigilance system (DDPS). Update of Summary of Product Characteristics	18/02/2010	23/03/2010	Annex II	With this variation the MAH submitted a new version of the DDPS (core version 8.0) in accordance with the current Pharmacovigilance guideline. After assessing the documentation the CHMP concluded that the submitted DDPS contained all required elements. Consequently, Annex II has been updated with the new version numb er of the agreed DDPS.
IB/0061	IB_33_Minor change in the manufacture of the finished product	01/02/2010	n/a		

IB/0060	IB_07_c_Replacement/add. of manufacturing site: All other manufacturing operations ex. batch release	01/02/2010	n/a		
II/0051	To amend section 4.8 of the hard capsules and oral solution SPCs to add the terms anxiety, delirium and pyrexia as common adverse events identified with use of Prometax patches. The package leaflets for the hard capsules and oral solution have been updated accordingly. The company also submitted an updated rivastigmine Detailed Description of the Pharmacovigilance system (DDPS) to Module 1.8.1. of the Prometax Marketing Authorisation, in accordance with the current pharmacovigilance guideline. Update of Summary of Product Characteristics and Package Leaflet	18/12/2008	26/01/2009	SmPC, Annex II and PL	Based on review of information from the published literature and the Novartis safety and clinical study databases, the MAH proposed that there is: a higher rate of Myocardial Infarction (MI) in the Prometax treatment group relative to placebo in Alzheimer's disease (AD) studies, no imbalance in the incidence of cerebrovascular accidents (CVA) in the overall Prometax group relative to placebo and a slight imbalance in the incidence of CVA with Prometax patch. In consequence, the following updates of the Prometax SPCs were initially proposed by the MAH: - 'myocardial infarction' is added as a rare adverse reaction (SPC section 4.8) of the Prometax oral formulations SPCs and referred to in the text of section 4.8 of the Prometax patch SPCs. - 'cerebrovascular accident' is added as an uncommon adverse reaction (SPC section 4.8) of Prometax patch SPCs and referred to in the text of section 4.8 of the Prometax oral formulations SPCs. - the adverse events 'anxiety', 'delirium', and 'pyrexia' are added in the SPC of Prometax hard capsules and oral formulation in section 4.8 as common adverse events occurring with Prometax patches. After assessing the data submitted by the MAH, the CHMP concluded that the results from provided studies are not

					robust enough either to justify addition of myocardial infarction event as a rare adverse reaction or cerebrovascular event as an uncommon adverse reaction in the SPCs of Prometax hard capsules and oral solution. Section 4.8 of the SPCs of Prometax hard capsules and oral formulation were amended to include the adverse events 'anxiety', 'delirium', and 'pyrexia' as common adverse events. The Detailed Description of the Pharmacovigilance system as described by the MAH (version 2.0) fulfils the legislative requirements as concluded by the CHMP and the Committee therefore recommended an update of Annex II accordingly.
IA/0057	IA_23_b_Change in source of excip./reagent to veg./synthetic material - other cases	15/12/2008	n/a		
IA/0056	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	12/12/2008	n/a		
IB/0054	IB_37_b_Change in the specification of the finished product - add. of new test parameter	03/12/2008	n/a		
IB/0053	IB_37_b_Change in the specification of the finished product - add. of new test parameter	03/12/2008	n/a		
IB/0052	IB_37_b_Change in the specification of the finished product - add. of new test parameter	03/12/2008	n/a		
IB/0055	IB_37_b_Change in the specification of the finished product - add. of new test parameter	26/11/2008	n/a		

IA/0050	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	03/06/2008	n/a		
R/0045	Renewal of the marketing authorisation.	19/03/2008	21/05/2008	SmPC, Annex II, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considered that the benefit/risk profile of Prometax continues to be favourable. The CHMP was also of the opinion that the renewal can be granted with unlimited validity.
IA/0046	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	04/02/2008	n/a		
X/0039	Annex I_2.(d) Change or addition of a new pharmaceutical form	19/07/2007	25/09/2007	SmPC, Labelling and PL	Please refer to the Scientific Discussion: Prometax H-255-X-39-SD.
N/0044	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/03/2007	n/a	PL	
II/0043	Change(s) to the test method(s) and/or specifications for the active substance	22/02/2007	28/02/2007		
II/0042	Change(s) to the manufacturing process for the active substance	22/02/2007	28/02/2007		
II/0037	This variation concerns an update of sections 4.4 and 4.8 of the SPC and section 4 of the PL in relation to	21/09/2006	24/10/2006	SmPC, Annex II, Labelling	Following the occurrence of 3 cases of oesophageal rupture, the product information was updated to highlight that in

	'Severe vomiting associated with oesophageal rupture' and 'Elevated liver function tests'. Update of Summary of Product Characteristics, Labelling and Package Leaflet			and PL	case of severe vomiting associated with rivastigmine treatment, appropriate dose adjustments as recommended in section 4.2 must be made. Some cases of severe vomiting were associated with oesophageal rupture. After a review of its Clinical and Safety database, the MAH updated the product information to add 'Severe vomiting associated with oesophageal rupture' with the frequency 'very rare'. Such events appeared to occur particularly after dose increments or high doses of rivastigmine. The frequency of 'Elevated liver function tests' was also modified from very rare to uncommon. In addition some clarifications have been introduced in section 5.1 of the SPC and the MAH also applied for a combined PL for the hard capsules, updated the annexes in accordance with the latest QRD template and introduced minor linguistic corrections in some of the languages.
IB/0041	IB_33_Minor change in the manufacture of the finished product	19/10/2006	n/a		
IB/0040	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IB_07_b_03_Replacement/add. of manufacturing site: Primary packaging site - liquid ph. forms	19/10/2006	n/a		
N/0038	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/07/2006	n/a	PL	
IA/0036	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	15/06/2006	n/a		

II/0033	Extension of Indication to include symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease. Extension of Indication	26/01/2006	02/03/2006	SmPC and PL	Please refer to Scientific Discussion: Prometax H-255-II-33-SD
IA/0035	IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	07/12/2005	n/a		
IA/0034	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	28/11/2005	n/a		
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/10/2004	n/a	Labelling and PL	
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/07/2004	n/a	PL	
IA/0030	IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	23/03/2004	n/a		
II/0028	New presentation(s)	17/12/2003	04/03/2004	SmPC, Labelling and PL	
II/0025	New presentation(s)	17/12/2003	04/03/2004	SmPC, Labelling and PL	
IA/0029	IA_32_a_Change in batch size of the finished product	03/03/2004	n/a		

	- up to 10-fold				
IA/0027	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	22/10/2003	n/a	Annex II and PL	
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/08/2003	22/09/2003	PL	
R/0023	Renewal of the marketing authorisation.	19/03/2003	26/06/2003	SmPC, Annex II, Labelling and PL	
I/0022	11_Change in or addition of manufacturer(s) of active substance	20/12/2002	n/a		
II/0021	Update of Summary of Product Characteristics and Package Leaflet	19/09/2002	18/12/2002	SmPC and PL	
II/0020	Update of Summary of Product Characteristics and Package Leaflet	27/06/2002	17/10/2002	SmPC and PL	
I/0019	01_Change following modification(s) of the manufacturing authorisation(s)	22/01/2002	05/03/2002	Annex II and PL	
I/0018	01_Change following modification(s) of the manufacturing authorisation(s)	22/01/2002	05/03/2002	Annex II and PL	
I/0016	20_Extension of shelf-life as foreseen at time of authorisation	03/10/2001	09/11/2001	SmPC	
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/10/2001	30/11/2001	PL	

II/0015	Update of Summary of Product Characteristics and Package Leaflet	25/04/2001	13/08/2001	SmPC and PL	
II/0012	Update of Summary of Product Characteristics and Package Leaflet	14/12/2000	20/03/2001	SmPC and PL	
I/0014	04_Replacement of an excipient with a comparable excipient	28/02/2001	13/03/2001		
I/0013	26_Changes to comply with supplements to pharmacopoeias	28/02/2001	13/03/2001		
I/0011	20_Extension of shelf-life as foreseen at time of authorisation	09/10/2000	18/12/2000	SmPC	
I/0010	20_Extension of shelf-life as foreseen at time of authorisation	09/10/2000	18/12/2000	SmPC	
X/0009	X-3-iv_Change or addition of a new pharmaceutical form	15/12/1999	11/05/2000	SmPC, Annex II, Labelling and PL	
II/0008	Update of Summary of Product Characteristics and Package Leaflet	14/12/1999	12/04/2000	SmPC, Labelling and PL	
I/0007	20_Extension of shelf-life as foreseen at time of authorisation	19/04/1999	02/07/1999	SmPC, Labelling and PL	
I/0006	17_Change in specification of the medicinal product	11/03/1999	19/03/1999		

I/0005	25_Change in test procedures of the medicinal product	11/03/1999	19/03/1999		
I/0004	15_Minor changes in manufacture of the medicinal product	11/03/1999	19/03/1999		
I/0002	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	11/03/1999	19/03/1999	Annex II and PL	
I/0001	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	11/03/1999	19/03/1999		