Mayzent

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
II/0032	Update of sections 5.1 and 4.8 of the SmPC in order to update efficacy and safety information from study CBAF312A2304 (EXPAND) listed as a category 3 study in the RMP. This is a phase III study and is comprised of two parts: a Core Part and an Extension Part. The Core Part was a multicenter,	27/03/2025		SmPC	Section 4.8 of the SmPC has been updated to inform that the safety-related information from the open-label extension part of the study A2304 (EXPAND) was consistent with that observed in the core part. Section 5.1 of the SmPC has been updated to inform about the percentage of patients who enrolled the open-label

[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).

	randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of siponimod in SPMS patients. This was followed by an open-label Extension Part, collecting long-term efficacy and safety data on siponimod for up to 7 years. In addition, the MAH took the opportunity to add editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				extension part of the study A2304 (EXPAND) and developed 6-month CDP at month 108. These exploratory results were presented for separately for patients initially allocated to siponimod in the core part of the study and for those who switched from placebo to siponimod after the core part. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10818 /202403	Periodic Safety Update EU Single assessment - siponimod	14/11/2024	13/01/2025	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10818/202403.
IAIN/0033	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	16/12/2024		Annex II and PL	
R/0029	Renewal of the marketing authorisation.	25/07/2024	19/09/2024	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety, and efficacy, the CHMP considered that the benefit-risk balance of Mayzent in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IA/0030	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	13/05/2024	19/09/2024	SmPC	
IAIN/0028/G	This was an application for a group of variations.	26/02/2024	n/a		

	A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites 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 A.7 - Administrative change - Deletion of manufacturing sites				
PSUSA/10818 /202303	Periodic Safety Update EU Single assessment - siponimod	09/11/2023	05/01/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/10818/202303.
IAIN/0027	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/12/2023	n/a		
IB/0026/G	This was an application for a group of variations. B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.d.z - Change in control of the Finished Product - Other variation	13/12/2023	n/a		
II/0023	Update of section 5.1 of the SmPC in order to present data on the effect of siponimod on delaying the progression to EDSS ≥7 (time-to-wheelchair) based on post-hoc analysis of study CBAF312A2304 (EXPAND). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/11/2023	19/09/2024	SmPC	Section 5.1 of the SmPC has been updated in order to present data on the effect of siponimod on delaying the progression to EDSS ≥7 (time-to-wheelchair) based on post-hoc analysis of study CBAF312A2304 (EXPAND). For more information, please refer to the Summary of Product Characteristics.
IA/0025/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 A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.a - Change to importer, batch release	07/09/2023	n/a		

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place				
IA/0024/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	25/08/2023	n/a		
II/0020	Update of sections 4.4 and 4.8 of the SmPC in order to add "Progressive multifocal leukoencephalopathy (PML)" to the list of adverse drug reactions (ADRs) with frequency "not know" based on post-marketing data. The Annex II (Physician's Checklist), and Package Leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the text regarding herpes viral infection in the Package Leaflet in alignment with the currently approved SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	06/07/2023	05/01/2024	SmPC and PL	Update of sections 4.4 and 4.8 of the SmPC in order to add "Progressive multifocal leukoencephalopathy (PML)" to the list of adverse drug reactions (ADRs) with frequency "not know" based on post-marketing data. The Annex II (Physician's Checklist), and Package Leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the text regarding herpes viral infection in the Package Leaflet in alignment with the currently approved SmPC. The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). For more information, please refer to the Summary of Product Characteristics.

IB/0021	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	05/04/2023	n/a		
PSUSA/10818 /202203	Periodic Safety Update EU Single assessment - siponimod	10/11/2022	12/01/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10818/202203.
PSUSA/10818 /202109	Periodic Safety Update EU Single assessment - siponimod	19/05/2022	18/07/2022	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10818/202109.
IG/1521	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	23/06/2022	n/a		
IA/0016/G	This was an application for a group of variations. B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.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	01/06/2022	n/a		

	size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size				
IB/0015/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	08/03/2022	n/a		
X/0007	Annex I_2.(c) Change or addition of a new strength/potency	16/12/2021	16/02/2022	SmPC, Labelling and PL	
II/0011/G	This was an application for a group of variations.	11/11/2021	16/02/2022	SmPC	For more information, please refer to the Summary of

	Update of section 4.5 of the SmPC to clarify the CYP2C9/CYP3A4 inhibitors/inducers information. Update of section 5.2 to add information regarding CYP2C9 genotypes less frequent alleles. Update of sections 4.4 and 4.5 of the SmPC to add information in case of administration of non-live attenuated vaccines, based on the vaccination study A2130. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				Product Characteristics.
PSUSA/10818 /202103	Periodic Safety Update EU Single assessment - siponimod	28/10/2021	n/a		PRAC Recommendation - maintenance
IAIN/0013/G	This was an application for a group of variations. 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.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 A.5.b - Administrative change - Change in the name	06/10/2021	16/02/2022	Annex II and PL	

	and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)				
IA/0012	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	06/08/2021	n/a		
IB/0009/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.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	13/07/2021	n/a		
PSUSA/10818 /202009	Periodic Safety Update EU Single assessment - siponimod	09/04/2021	n/a		PRAC Recommendation - maintenance
IA/0006/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of	22/01/2021	n/a		

	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				
PSUSA/10818 /202003	Periodic Safety Update EU Single assessment - siponimod	12/11/2020	07/01/2021	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10818/202003.
IAIN/0004	B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	21/08/2020	07/01/2021	Annex II and PL	
IB/0002/G	This was an application for a group of variations. B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	02/04/2020	07/01/2021	SmPC, Labelling and PL	
IAIN/0001	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	17/02/2020	07/01/2021	SmPC, Labelling and PL	