Ponvory

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/0018/G	This was an application for a group of variations. Grouped application comprised of two Type II Variations, as follows: C.I.13: Submission of the final report from study AC-058B202; this is a Multicenter, Randomized, Double-	04/09/2025	12/02/2026	SmPC	Section 5.1 is being updated as follows: Patients with RMS who completed the phase 3 OPTIMUM study were eligible to enter the exploratory, open-label extension study OPTIMUM-LT. In total, 877 patients were enrolled (i.e., 77.4% of patients from OPTIMUM; n=439 from ponesimod arm and n=438 from teriflunomide arm). All patients

[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).

	blind, Parallel-group Extension to Study AC-058B201 to Investigate the Long-term Safety, Tolerability, and Efficacy of 10, 20, and 40 mg/day Ponesimod, an Oral S1P1 Receptor Agonist, in Patients with Relapsing-remitting Multiple Sclerosis. C.I.13: Submission of the final report from study AC-058B303 (OPTIMUM-LT); this is a Multicenter, Non-Comparative Extension to Study AC-058B301, to Investigate the Long- Term Safety, Tolerability, and Control of Disease of Ponesimod 20 mg in Subjects with Relapsing Multiple Sclerosis. Section 5.1 of the SmPC is updated. The RMP is also updated to version 4.1. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				received ponesimod 20 mg once daily for up to 240 weeks. The mean treatment duration was 46.91 months (range: 0.7–71.8 months) and drop-out rate was 25.4%. The mean ARR in the extension period was 0.132 (95% CLs: 0.113, 0.152). At Week 384, the Kaplan Meier estimate of patients with a 24-week CDA in the extension study, continuously treated with ponesimod (P20 mg/P20 mg) since core study randomization, was 21.3% (95% CLs: 17.7, 25.6). For more information, please refer to the Summary of Product Characteristics.
T/0017	Transfer of Marketing Authorisation	21/08/2024	09/10/2024	SmPC, Labelling and PL	
PSUSA/10940 /202403	Periodic Safety Update EU Single assessment - ponesimod	03/10/2024	n/a		PRAC Recommendation - maintenance
II/0013	Update of section 4.4 of the SmPC to amend an existing warning on PML-IRIS based on the cumulative review of literature. In addition, the MAH took the opportunity to introduce editorial changes to	25/07/2024	09/10/2024	SmPC	Section 4.4 subsection Progressive multifocal leukoencephalopathy is updated to inform that immune reconstitution inflammatory syndrome (IRIS) has not been reported with Ponvory, but it has been reported in patients

	the PI and to bring the PI in line with the latest QRD template version 10.3. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				treated with S1P receptor modulators who developed PML and subsequently discontinued treatment. IRIS presents as a clinical decline in the patient's condition that may be rapid, can lead to serious neurological complications or death, and is often associated with characteristic changes on MRI. The time to onset of IRIS in patients with PML was generally within four months after S1P receptor modulator discontinuation. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken. Section 4.4 subsection return of disease activity after ponesimod discontinuation has been updated to inform that after stopping Ponvory in the setting of PML, monitor for development of immune reconstitution inflammatory syndrome (PML-IRIS). For more information, please refer to the Summary of Product Characteristics.
IB/0015	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	09/04/2024	n/a		
II/0014	Update of section 4.5 of the SmPC to amend an existing interaction wording for carbamazepine under the sub-heading "Effect of other medicinal products on ponesimod" based on study 67896153MSC1001. This is a Phase 1, Open-label, Parallel-group Study to Assess the Effect of Steady-state Carbamazepine on the Pharmacokinetics of Ponesimod in Healthy Adult Participants. In addition, the MAH took the opportunity to update the contact details of local representatives in the Package Leaflet.	08/02/2024	09/10/2024	SmPC and PL	Section 4.5 of the SmPC has been amended to inform that no dose adjustment is needed when ponesimod is co-administered with strong CYP3A4 and UGT1A1 inducers. For more information, please refer to the Summary of Product Characteristics.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10940 /202303	Periodic Safety Update EU Single assessment - ponesimod	26/10/2023	n/a		PRAC Recommendation - maintenance
IB/0012	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	28/07/2023	n/a		
PSUSA/10940 /202209	Periodic Safety Update EU Single assessment - ponesimod	26/04/2023	04/07/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10940/202209.
IB/0010	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	06/02/2023	n/a		
PSUSA/10940 /202203	Periodic Safety Update EU Single assessment - ponesimod	27/10/2022	n/a		PRAC Recommendation - maintenance
IB/0008	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	01/07/2022	n/a		
IB/0006	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	30/05/2022	15/03/2023	SmPC	
PSUSA/10940	Periodic Safety Update EU Single assessment -	07/04/2022	n/a		PRAC Recommendation - maintenance

/202109	ponesimod				
IB/0005	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	15/03/2022	15/03/2023	SmPC, Labelling and PL	
IB/0004/G	This was an application for a group of variations. 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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	28/02/2022	n/a		
IB/0002	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	03/12/2021	n/a		