Raxone

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
IB/0040/G	This was an application for a group of variations. 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	26/06/2024	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).

	material/intermediate B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue				
IB/0037/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - 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 A.7 - Administrative change - Deletion of manufacturing sites	07/05/2024	n/a		
IAIN/0039/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation 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	23/04/2024		SmPC, Annex II and PL	

	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.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				
PSUSA/10412 /202309	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	11/04/2024	n/a		PRAC Recommendation - maintenance
IA/0038	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	11/03/2024	n/a		
S/0035	8th annual re-assessment	22/02/2024	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Raxone should be maintained.
T/0034	Transfer of Marketing Authorisation	22/09/2023	19/10/2023	SmPC, Labelling and PL	

PSUSA/10412 /202209	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	14/04/2023	n/a		PRAC Recommendation - maintenance
S/0032	7th annual re-assessment	23/02/2023	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Raxone should be maintained.
II/0031	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/07/2022	07/07/2023	SmPC and Annex II	
S/0029	6th annual re-assessment	19/05/2022	15/07/2022	SmPC, Annex II and PL	The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Raxone should be varied.
PSUSA/10412 /202109	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	07/04/2022	n/a		PRAC Recommendation - maintenance
IB/0028	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	21/07/2021	15/07/2022	Annex II	
IB/0027/G	This was an application for a group of variations. 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.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished	25/05/2021	n/a		

	product - Deletion of a non-significant in-process test B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
PSUSA/10412 /202009	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	09/04/2021	n/a		PRAC Recommendation - maintenance
S/0023	Annual re-assessment.	25/03/2021	n/a		
IB/0024/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.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any	06/01/2021	n/a		

	manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products				
R/0020	Renewal of the marketing authorisation.	28/05/2020	06/08/2020	SmPC, Annex II, Labelling and PL	
PSUSA/10412 /201909	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	17/04/2020	n/a		PRAC Recommendation - maintenance
S/0019	The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Raxone should be maintained.	27/02/2020	n/a		
II/0018	Submission of the final report from study SNT-EAP-001 listed as a Specific Obligation (SOB11, former SOB4) in the Annex II of the Product Information. This is a follow-up study of patients in the Expanded Access Program (SNT-EPA-001) for Raxone in the treatment of patients with Leber's Hereditary Optic Neuropathy (LHON). The goal is to collect further long-term real-world efficacy and safety data. Annex II is modified accordingly. An updated RMP version 1.9 submitted accordingly. The requested variation proposed amendments to the Annex II and to the Risk Management Plan	14/11/2019	04/05/2020	Annex II	

	(RMP). C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
II/0016	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	17/10/2019	04/05/2020	Annex II	The applicant submitted final results from the SNT-CRS-002 listed as a Specific Obligation (SOB10, former SOB2) which is a Historical case record survey (CRS) of visual acuity data from patients with Leber's hereditary optic neuropathy (LHON) to be used as the external control to the open label study. After completion of the SOB, this SOB was deleted from Annex IIE in the PI as well as from the RMP.
IAIN/0017	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	27/08/2019	n/a		
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	28/05/2019	04/05/2020	Annex II	
PSUSA/10412 /201809	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	11/04/2019	n/a		PRAC Recommendation - maintenance
S/0012	Annual re-assessment.	28/02/2019	n/a		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/12/2018	07/02/2019	Labelling	
IAIN/0011/G	This was an application for a group of variations.	19/10/2018	n/a		

	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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) A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
PSUSA/10412 /201709	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	12/04/2018	n/a		PRAC Recommendation - maintenance
II/0008	Update of SmPC section 4.5 to amend an existing warning in relation to CY3A4 substrates based on the final report of study SNT-I-017: An open-label study to assess the potential for pre-systemic inhibition of cytochrome P450 3A4 (CYP3A) by idebenone in healthy male subjects using midazolam as a substrate. The Package Leaflet was updated accordingly. An updated RMP version 1.5 was submitted as part of the application. The provision of the study report addresses the post-authorisation measure MEA 005.1.	08/03/2018	07/02/2019	SmPC and PL	In vivo idebenone is a mild inhibitor of CYP3A4. Data from a drug-drug interaction study in 32 healthy volunteers indicate that on the first day of oral administration of 300 mg idebenone t.i.d., the metabolism of midazolam, a CYP3A4 substrate, was not modified when both drugs were administered together. After repeated administration Cmax and AUC of midazolam were increased by 28% and 34%, respectively, when midazolam was administered in combination with 300 mg idebenone t.i.d. Therefore, CYP3A4 substrates known to have a narrow therapeutic index such as alfentanil, astemizole, terfenadine, cisapride, cyclosporine, fentanyl, pimozide, quinidine, sirolimus,

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				tacrolimus, or ergot alkaloids (ergotamine, dihydroergotamine) should be administered with caution in patients receiving idebenone.
S/0009	2nd annual re-assessment	22/02/2018	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Raxone should be maintained.
S/0005	1st Annual Re-assessment	21/04/2017	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that the Marketing Authorisation of Raxone should be maintained.
IB/0007	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	18/04/2017	n/a		
PSUSA/10412 /201609	Periodic Safety Update EU Single assessment - idebenone (centrally authorised products)	06/04/2017	n/a		PRAC Recommendation - maintenance
IA/0004	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	12/08/2016	19/07/2017	SmPC	
II/0002	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	28/04/2016	n/a		