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
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/12/2018		Labelling	
IAIN/0011/G	This was an application for a group of variations. 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	19/10/2018	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).

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	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. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	08/03/2018		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, 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		