Rasagiline ratiopharm

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/0020	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/10/2021		Labelling and PL	
WS/2011	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	09/04/2021	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).

	Submission of an updated RMP (version 3.1) following the completion of study TV1030-CNS-50024 (listed as a category 3 study in the RMP): a non-interventional retrospective cohort study which was conducted using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagiline mesylate in patients with Parkinson's disease (as assessed and concluded in procedure WS/1749 finalised in September 2020). The MAH took the opportunity to introduce a minor update to the targeted follow-up questionnaire for the important potential risk of malignant melanoma and to revise the list of safety concerns in line with GVP Module V revision 2.0.1. 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				
WS/1749	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final report from study TV1030-CNS-50024 listed as a category 3 study in the RMP. This is a non-interventional retrospective cohort study which was conducted using the United States	03/09/2020	23/09/2021	SmPC and PL	The SmPC section 4.4 was updated to include the results of a retrospective cohort study which suggested a possibly increased risk of melanoma with the use of rasagiline, especially in patients with longer duration of rasagiline exposure and/or with the higher (1mg) dose of rasagiline. Any suspicious skin lesion should be evaluated by a specialist. Patients should therefore be advised to seek immediate medical review if a new or changing skin lesion is

	Medicare research database to assess the potential risk of melanoma associated with the use of rasagilline mesylate in patients with Parkinson's disease. Section 4.4. of SmpC was updated to amend the information on the risk of melanoma associated with the use of rasagiline. The package leaflet is updated in accordance. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				identified. For more information, please refer to the Summary of Product Characteristics.
WS/1789/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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	17/04/2020	n/a		
WS/1771/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.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	12/03/2020	n/a		

	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation				
R/0014	Renewal of the marketing authorisation.	25/07/2019	06/09/2019	Labelling and PL	
PSUSA/2612/ 201901	Periodic Safety Update EU Single assessment - rasagiline	05/09/2019	n/a		PRAC Recommendation - maintenance
IA/0013	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)	07/03/2019	n/a		
WS/1361	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	21/06/2018	26/07/2018	SmPC, Labelling and PL	
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/01/2018	26/07/2018	PL	
WS/1168	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, 4.7 and 4.8 to include a new warning on excessive daytime sleepiness and sudden	01/09/2017	26/07/2018	SmPC, Annex II, Labelling and PL	Based on new available Pharmacovigilance data, a signal of sudden onset of sleep/sleep attack was raised. Excessive daily sleepiness (hypersomnia, lethargy, sedation, sleep attacks, somnolence, sudden onset of sleep) can occur in patients treated with dopamine agonists and/or other dopaminergic treatments. A similar pattern of excessive daily

	sleep onset episodes, update of section 4.9 to remove 'dysphoria' as a symptom reported following overdose of rasagiline based on a CCDS update. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to make editorial changes throughout the PI, to correct the invented name for Rasagiline Ratiopharm in the Czech annexes and to bring the PI in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				sleepiness has been reported post-marketing with rasagiline. Although many of these patients reported somnolence while on rasagiline with other dopaminergic medicinal products, some perceived that they had no warning signs, such as excessive drowsiness, and believed that they were alert immediately prior to the event. Some of these events have been reported more than 1-year after initiation of treatment. In patients experiencing somnolence/sudden sleep episodes, rasagiline may have major influence on the ability to drive and use machines. Patients should be cautioned about operating hazardous machines, including motor vehicles, until they are reasonably certain that rasagiline does not affect them adversely. Patients being treated with rasagiline and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from driving or engaging in activities where impaired alertness may put themselves or others at risk of serious injury or death (e.g. operating machines) until they have gained sufficient experience with rasagiline and other dopaminergic medications to gauge whether or not it affects their mental and/or motor performance adversely. In addition as the term 'dysphoria' can be attributed to cognitive effects of serotonin syndrome, it was removed from the list of symptoms reported following overdose of rasagiline in doses ranging from 3 mg to 100 mg.
IG/0789/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	18/04/2017	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method				
WS/0984	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	09/02/2017	n/a		
WS/0985/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.b - Change in the specification parameters and/or limits of an AS, starting	27/10/2016	n/a		

	material/intermediate/reagent - Tightening of specification limits 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				
PSUSA/2612/201601	Periodic Safety Update EU Single assessment - rasagiline	02/09/2016	n/a		PRAC Recommendation - maintenance
IG/0648/G	This was an application for a group of variations. 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	15/01/2016	n/a		
IAIN/0004/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	23/09/2015	01/08/2016	SmPC, Labelling and PL	

IAIN/0003/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.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	23/09/2015	01/08/2016	SmPC, Annex II, Labelling and PL	
WS/0767/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.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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 manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP -	06/08/2015	01/08/2016	Annex II and PL	

	Including batch control/testing B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
IB/0001	B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	27/03/2015	n/a		