Levodopa/Carbidopa/Entacapone Orion

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/0041	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/01/2025		PL	
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/03/2024		PL	

[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).

IG/1611/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	18/05/2023	n/a		
IG/1580	A.7 - Administrative change - Deletion of manufacturing sites	12/01/2023	25/01/2024	Annex II and PL	
PSUSA/547/202110	Periodic Safety Update EU Single assessment - carbidopa / entacapone / levodopa	10/06/2022	n/a		PRAC Recommendation - maintenance
WS/2202/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.z - Quality change - Active substance - Other variation 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	31/03/2022	n/a		

	an obsolete parameter) B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IG/1495	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	14/03/2022	n/a		
WS/2175	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	27/01/2022	16/12/2022	SmPC, Labelling and PL	
WS/2105/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.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition) B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	25/11/2021	n/a		

	or addition) for the AS or a starting material/intermediate 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				
WS/2124/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.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.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	16/09/2021	n/a		
IG/1408/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	17/06/2021	n/a		

	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
IG/1303	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	25/11/2020	01/07/2022	SmPC, Annex II, Labelling and PL	
WS/1735/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.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) B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	12/03/2020	n/a		
WS/1667/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.	05/12/2019	n/a		

	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.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/547/201810	Periodic Safety Update EU Single assessment - carbidopa / entacapone / levodopa	29/05/2019	08/08/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/547/201810.
IG/1060	A.7 - Administrative change - Deletion of manufacturing sites	28/02/2019	n/a		
IG/0965/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.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	23/10/2018	n/a		
WS/1327	This was an application for a variation following a	08/02/2018	08/08/2019	SmPC,	

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation			Labelling and PL	
IG/0867	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	20/11/2017	n/a		
IG/0858/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	30/10/2017	n/a		
IG/0807	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)	10/08/2017	n/a		

R/0019	Renewal of the marketing authorisation.	01/04/2016	26/05/2016		Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Levodopa/Cabidopa/Entacapone Orion in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/547/201510	Periodic Safety Update EU Single assessment - carbidopa / entacapone / levodopa	13/05/2016	n/a		PRAC Recommendation - maintenance
IG/0631/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	04/12/2015	n/a		

	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/09/2015		PL	
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/06/2015	22/01/2016	PL	
IG/0546	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	27/04/2015	n/a		
WS/0665	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To update the Product Information as follows: - to include ADR statement - to update the PI to QRD template version 9 - to include an explanation to the PL of the pictogram which is currently only displayed on the carton (all products except Comtan) - to correct the local contact information for Malta in Stalevo PL - to correct the local contact information for Latvia in all PLs except for Comtan and Entacapone Orion - to correct the local contact information for Germany in Comtess and	22/01/2015	22/01/2016	SmPC, Labelling and PL	

	Levodopa/Carbidopa/Entacapone Orion - for Comtan only: to add 'Magnesium stearate' to the list of excipients for the film-coating in the SmPC and PL. Tablet core and Film-coating both contain magnesium stearate - to correct linguistic amendments in Annexes - to amend a mistake in the Annex A (only for Comtan). C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
WS/0651	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To include an additional analytical method for the active substance carbidopa. 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	18/12/2014	n/a		To include an additional analytical method for the active substance carbidopa.
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/06/2014	22/01/2016	PL	
IG/0433/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging	08/05/2014	n/a		

	site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IAIN/0010/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	17/03/2014	n/a		
IG/0415/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	13/03/2014	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/08/2013	22/01/2016	PL	
X/0003	Annex I_2.(c) Change or addition of a new strength/potency	25/04/2013	27/06/2013	SmPC, Labelling and PL	
IA/0007	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	13/05/2013	n/a		
IG/0302/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new or updated Ph. Eur.	13/05/2013	n/a		

	Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer 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				
WS/0331	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC sections 4.4 and 4.8 in order to update the safety information by implementing class labelling for the risk of impulse control disorders. C.I.3.z - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Other variation	13/12/2012	14/01/2013	SmPC, Annex II, Labelling and PL	Based on a recent review of the available post-marketing data in relation to the risk of development of impulse control disorders when using medicinal products containing levodopa, dopamine agonists and/or catechol-O-methyltransferase (COMT) inhibitors, the CHMP/PhVWP requested a class labelling to update and harmonise the product information of all products concerned. In response to this request, the product information was updated to reflect behavioural symptoms related to impulse control disorders including compulsive spending or buying, binge eating and compulsive eating. It was clarified that this adverse reaction can occur irrespective of the indication and at normal doses. Furthermore, regular monitoring of patients and a careful review of treatment, if symptoms occur, is recommended. The Package Leaflet was updated in accordance and advice for the patient's family and carers was provided.
IG/0229	B.III.1.a.3 - Submission of a new or updated Ph. Eur.	09/11/2012	n/a		

	Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)				
WS/0199	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.III.2.a.1 - Change of specification('s) of a former non Pharmacopoeial substance to comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS	19/01/2012	19/01/2012		
IG/0110	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	04/10/2011	n/a		