EMA/126228/2021

DaTSCAN

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/0059	C.I.4, Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to describe the possibility of quantitative reading in line with current scientific knowledge.	28/01/2021		SmPC	In Section 4.4, text on the interpretation of DaTSCAN images is added, with a conclusion that final assessment should always consider both visual appearance and semi-quantitative results. In section 5.1, the evidence regarding the semi-quantitative reading is summarised.

[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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	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				For more information, please refer to the Summary of Product Characteristics.
II/0060	Submission of the first RMP. 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	26/11/2020	n/a		
IB/0058	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	25/09/2019	n/a		
T/0057	Transfer of Marketing Authorisation	12/12/2018	05/03/2019	SmPC, Labelling and PL	
IA/0056	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	26/10/2018	n/a		
II/0055	Update of section 4.8 of the SmPC in order to add, as side effects, erythema, pruritus, rash, urticaria, hyperhidrosis, dyspnea, vomiting, blood pressure decreased and 'feeling hot' with a not known frequency and 'burning sensation' with an uncommon	19/07/2018	05/03/2019	SmPC, Labelling and PL	

	frequency. The Package leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 11 of the SmPC in line with ICRP Publication 128, Radiation Dose to Patients from "Radiopharmaceuticals: a Compendium of Current Information Related to Frequently Used Substances, 2015". The Marketing authorisation holder (MAH) took also the opportunity to bring the PI in line with the latest QRD template version 10.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0054/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products 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.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	03/05/2018	n/a		

PSUSA/1767/ 201707	Periodic Safety Update EU Single assessment - ioflupane (123i)	08/03/2018	n/a		PRAC Recommendation - maintenance
IB/0053	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	15/02/2018	n/a		
IB/0051/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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 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.b.1.d - Change in the specification parameters and/or limits of an AS, starting	23/01/2017	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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				
IAIN/0050/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	17/08/2016	09/01/2017	Annex II, Labelling and PL	
IB/0049	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/06/2016	09/01/2017	SmPC, Annex II, Labelling and PL	
IB/0048/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of	26/01/2016	09/01/2017	SmPC	

	manufacturing sites B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation 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)				
IAIN/0047	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	11/11/2013	n/a		
IB/0044	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the currently approved batch size	29/07/2013	n/a		
IB/0045/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	16/07/2013	n/a		

	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/07/2013	09/01/2017	PL	
IA/0042/G	This was an application for a group of variations. 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 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)	21/05/2013	n/a		
IA/0041/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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 B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	12/04/2013	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
II/0040	Update of section 4.1 of the SmPC in order to clarify in the target population of patients with clinically uncertain Parkinsonian Syndromes that these may include patients with early symptoms. Furthermore, Annex II of the PI was brought in line with the latest QRD template version 8.3. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	21/02/2013	22/03/2013	SmPC and Annex II	Based on the review of available clinical data, including results from a study in patients with early signs and symptoms of movement disorders, the CHMP concluded that DaTSCAN was effective as a diagnostic tool to detect loss of functional dopaminergic neurons in the brain of patients with clinically uncertain Parkinsonian Syndromes presenting with early symptoms. This review was performed following a request from the CHMP. A clarification of the approved target population to include uncertain case of early Parkinsonian symptoms was implemented in section 4.1 of the SmPC.
IA/0039	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	21/09/2012	n/a		
IA/0038	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	01/08/2012	n/a		
II/0037	The MAH proposes to change section 5.3 of the current Datscan SmPC by revising the toxicity information provided to focus on the most important aspects. This change is a follow-up measure as part of the MAH's post approval undertaking for renewal procedure EMEA/H/C/266/R/0033.	17/03/2011	18/04/2011	SmPC	The MAH has proposed to amend section 5.3 of the current Datscan SmPC by revising the toxicity information provided in this section. The following text will be included in section 5.3: "Non-clinical data for ioflupane reveal no special hazard for humans based on conventional studies of safety

	C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				pharmacology, single and repeated dose toxicity and genotoxicity. Studies on reproductive toxicity and to assess the carcinogenic potential of ioflupane have not been performed."
II/0036	The MAH proposes to update section 4.8 of the current SmPC and corresponding section of the PL with addition of reported adverse drug reactions and amended frequencies for existing undesirable effects based upon current data. This change is a follow-up measure as part of the MAH's post approval undertaking for renewal procedure EMEA/H/C/266/R/0033. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	17/03/2011	18/04/2011	SmPC and PL	The MAH has submitted a variation to update section 4.8 of the SmPC and the corresponding section of the PL with additional adverse drug reactions (ADRs) and changes in frequency for currently included ADRs based on data from clinical trials with Datscan. This change is a follow up measure included in the MAH's post approval undertaking for a recent renewal procedure. The adverse reactions dizziness, nausea, dry mouth and dysgeusia have been added to section 4.8 of the SmPC with frequency 'uncommon'. The PL has been amended accordingly.
II/0035	Type II variation related to section 4.2 of the SmPC to remove the recommendation for application of thyroid blockade to patients 12 to 24 hours after administration of Datscan. This change is a follow-up measure as part of the MAHs post approval undertaking for renewal procedure EMEA/H/C/266/R/0033.	17/03/2011	18/04/2011	SmPC	As a result of this type II variation, the recommendation for application of thyroid blockade to patients 12 to 24 hours after administration of Datscan has been removed from section 4.2 of the SmPC. The recommendation for an application of thyroid blockade 1 to 4 hours prior to injection remains, however.

	C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				
II/0034/G	This was an application for a group of variations. Replacement of the manufacturing site for container closure sytem preparation with subsequent change in the manufacturing process of the finished product B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products	22/07/2010	06/08/2010		
R/0033	Renewal of the marketing authorisation.	20/05/2010	28/07/2010	SmPC, Annex II, Labelling and PL	
IB/0032	IB_10_Minor change in the manufacturing process of	14/08/2009	n/a		

	the active substance				
IB/0031	IB_10_Minor change in the manufacturing process of the active substance	14/08/2009	n/a		
IB/0030	IB_38_c_Change in test procedure of finished product - other changes	20/11/2008	n/a		
IB/0029	IB_33_Minor change in the manufacture of the finished product IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	20/11/2008	n/a		
II/0026	Minor editorial updates of Summary of Product Characteristics and list of local representatives and major revisisons to the Package Leaflet resulting from User Testing. Update of Summary of Product Characteristics and Package Leaflet	22/03/2007	24/04/2007	SmPC and PL	The MAH has revised the Package leaflet with results from user testing. The user testing was adequately conducted according to the guidelines for consultations with target patient groups 'user testing'. The CHMP considered that the amended Package Leaflet is legible, clear and easy to use and complies with the QRD template.
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/11/2006	n/a	PL	
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/10/2006	n/a	Labelling and PL	
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/10/2006	n/a	PL	
IA/0021	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	15/08/2006	n/a	Annex II and	

	IA_05_Change in the name and/or address of a manufacturer of the finished product			PL	
IA/0022	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	08/08/2006	n/a		
II/0020	Change(s) to the manufacturing process for the finished product	28/06/2006	03/07/2006		
II/0018	Extension of Indication	28/06/2006	03/07/2006	SmPC, Annex II and PL	The Indication has been extended in order to help differentiate probable dementia with Lewy bodies from Alzheimer's disease. For further information, please refer to Scientific Discussion document (DaTSCAN-H-266-AR-II-18).
II/0019	Quality changes	01/06/2006	06/06/2006		
IB/0017	IB_10_Minor change in the manufacturing process of the active substance	14/12/2005	n/a		
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/11/2005	n/a	PL	
IB/0015	IB_33_Minor change in the manufacture of the finished product IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	03/11/2005	n/a	SmPC, Annex II, Labelling and PL	
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/09/2005	n/a	PL	
IB/0013	IB_14_b_Change in manuf. of active substance	08/09/2005	n/a		

	without Ph. Eur. certificate - new manufacturer				
R/0011	Renewal of the marketing authorisation.	23/06/2005	07/09/2005	SmPC, Annex II, Labelling and PL	
IA/0012	IA_01_Change in the name and/or address of the marketing authorisation holder	16/06/2005	n/a	SmPC, Labelling and PL	
II/0010	Update of Summary of Product Characteristics, Labelling and Package Leaflet	20/01/2005	28/02/2005	SmPC, Labelling and PL	
N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/05/2004	n/a	PL	
N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/12/2003	20/01/2004	PL	
II/0006	Change(s) to the manufacturing process for the finished product	21/11/2002	29/11/2002		
II/0005	Update of Summary of Product Characteristics and Package Leaflet	25/07/2002	28/10/2002	SmPC and PL	
II/0003	Update of Summary of Product Characteristics and Package Leaflet	27/06/2002	09/09/2002	SmPC and PL	
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/08/2002	17/10/2002	PL	
I/0004	03_Change in the name and/or address of the	25/03/2002	07/05/2002	SmPC, Annex	

	marketing authorisation holder 01_Change in the name of a manufacturer of the medicinal product			II, Labelling and PL	
I/0002	20a_Extension of shelf-life or retest period of the active substance	19/03/2001	02/04/2001		
II/0001	New presentation(s)	19/10/2000	22/02/2001	SmPC, Labelling and PL	