Inovelon

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/0065	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/02/2023		PL	
IAIN/0064/G	This was an application for a group of variations. B.IV.1.a.1 - Change of a measuring or administration	08/12/2022	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).

	device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method				
IA/0063	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	08/07/2022	n/a		
N/0062	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/07/2021		PL	
IA/0061	A.7 - Administrative change - Deletion of manufacturing sites	17/03/2021	17/06/2021	Annex II and PL	
IA/0060/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 A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	08/10/2020	n/a		

PSUSA/2671/202001	Periodic Safety Update EU Single assessment - rufinamide	03/09/2020	n/a		PRAC Recommendation - maintenance
IB/0059	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	10/08/2020	n/a		
N/0055	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/07/2020	17/06/2021	PL	
IG/1263	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	24/06/2020	17/06/2021	Annex II and PL	
IG/1260/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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	24/06/2020	17/06/2021	SmPC, Labelling and PL	
IB/0056/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	08/06/2020	n/a		

	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
IA/0053/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/02/2020	n/a		
II/0052	Update of section 4.2 and 6.6 of the SmPC in order to include an additional method of administration via feeding tube for Inovelon oral suspension. This fulfills the CHMP recommendation to evaluate the feasibility of administrating the rufinamide oral suspension via an enteral feeding tube adopted with variation II/45. The RMP version 11 has been submitted. The requested variation proposed amendments to the Summary of Product Characteristics and to the Risk Management Plan (RMP). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/06/2019	31/07/2019	SmPC	The SmPC section 4.2 has been updated to include an additional method of administration via feeding tube for Inovelon oral suspension.
IAIN/0051/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	13/03/2019	n/a		

	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking				
IG/1044/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.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	22/01/2019	n/a		
IG/1008	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	30/11/2018	31/07/2019	Annex II and PL	
T/0048	Transfer of Marketing Authorisation	30/08/2018	21/09/2018	SmPC, Labelling and PL	
II/0045	Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients 1 year of age and older as adjunctive	28/06/2018	03/08/2018	SmPC, Labelling and	For further details please refer to the Scientific Discussion Inovelon EMEA/H/C/000660/II/0045.

	therapy; as a consequence sections 4.1, 4.2, 4.5, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet and the RMP (version 10.0) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections with the Product Information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the Product Information is brought in line with the latest QRD template version 10. The variation leads to amendments to the Summary of Product Characteristics, Labelling and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one			PL	
IAIN/0047	B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	04/07/2018	n/a		
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/11/2017	03/08/2018	PL	
PSUSA/2671/ 201701	Periodic Safety Update EU Single assessment - rufinamide	01/09/2017	n/a		PRAC Recommendation - maintenance
II/0041	Submission of the final clinical study report for study E2080-E044-401, the European registry of anti-epileptic drug use in patients with Lennox-Gastaut	06/07/2017	n/a		This non-interventional study E2080-E044-401 aimed at evaluating the long-term safety of rufinamide and seizure control during follow-up. Considering the limited number of

	Syndrome (LGS), listed as a category 3 study in the RMP, in order to fulfil MEA 002.1. This is a non-interventional EU registry study entering patients (aged ≥4 years) with LGS who required a modification in anti-epileptic therapy (either the addition of another AED or the change of one drug to another) to evaluate the long-term safety of rufinamide. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				patients enrolled in the study, the efficacy results are considered informative but not conclusive. They provided interesting qualitative information on the LGS response to different treatment in a non-interventional use and no significant differences between rufinamide group and other anti-epileptic drugs were observed. The safety profile in this study was consistent with the known safety profile of rufinamide. Overall, the results presented are consistent with the know efficacy and safety profile of Inovelon and did not warrant amendment to the product information.
N/0044	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/04/2017	03/08/2018	PL	
IA/0042	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	23/03/2017	n/a		
II/0037	Update of sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC in order to include additional information relevant to the paediatric population based on the results of study 303 in patients aged 1 to less than 4 years with Lennox-Gastaut Syndrome and the results from toxicity studies in juvenile animals. Section 5.1 was furthermore updated to add additional information on the design of study 022 in LGS patients aged 4 years and older. Additional editorial amendments were made to SmPC sections 4.4 and 4.6. The Package Leaflet has been updated	15/12/2016	11/01/2017	SmPC, Labelling and PL	Please refer to the Scientific Discussion Inovelon EMEA/H/C/000660/II/0037.

	accordingly. Furthermore, the PI was brought in line with the latest QRD template and the SmPCs, labelling and Package Leaflets for the three authorised strengths of the tablet formulation were combined. An updated RMP version 9.0 was agreed as part of the procedure. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0040	Submission of the final clinical study report for study E2080-A001-502, a phase V open-label non-interventional study to assess the palatability and acceptability of rufinamide oral suspension for the treatment of patients with Lennox-Gastaut syndrome aged 1 to 12 years old, in line with the agreed PIP. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/09/2016	n/a		
PSUSA/2671/ 201601	Periodic Safety Update EU Single assessment - rufinamide	02/09/2016	n/a		PRAC Recommendation - maintenance
IA/0039/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	28/06/2016	n/a		

	manufacturer of a novel excipient 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 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.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				
IA/0036/G	This was an application for a group of variations. B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms	30/10/2015	n/a		
PSUSA/2671/ 201501	Periodic Safety Update EU Single assessment - rufinamide	10/09/2015	n/a		PRAC Recommendation - maintenance
IB/0035	To replace the particle size in-process test (IPC) using a laser diffraction method by an IPC test using an analytical sieving method for Inovelon Oral	14/08/2015	n/a		

	Suspension manufactured at Patheon B.II.b.5.f - Change to in-process tests or limits applied during the manufacture of the finished product - Addition or replacement of an in-process test as a result of a safety or quality issue				
IA/0033/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	03/12/2014	n/a		
IB/0032/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 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.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.3.f - Change in the manufacturing process of	02/10/2014	n/a		

	the finished or intermediate product - Minor change in the manufacturing process of an aqueous oral suspension 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.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
PSUV/0030	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
IA/0031	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)	30/06/2014	n/a		
PSUV/0029	Periodic Safety Update	06/02/2014	n/a		PRAC Recommendation - maintenance

IG/0345	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	03/09/2013	n/a		
IB/0027	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)	28/06/2013	13/12/2013	SmPC, Annex II, Labelling and PL	
IAIN/0026	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/02/2013	n/a		
II/0025	Further to the assessment of PSUR No 7 a type II variation was submitted to specifically mention DRESS and Stephens-Johnson syndrome to the current warning of serious hypersensivity reaction of Section 4.4 of the SmPC. Additionally, section 4.5 of the tablets SmPC was updated to reflect that rufinamide appears not to have a clinically relevant effect on phenytoin concentration, in line with the information already included in the oral suspension. 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	15/11/2012	13/12/2013	SmPC and PL	Further to the assessment of PSUR No 7 the CHMP requested to the MAH to specifically mention DRESS and Stephens-Johnson syndrome to the current warning of serious hypersensivity reaction of Section 4.4 of the SmPC. In addition, discrepancies were noted between the CCDS and the EU SmPC in section 4.5 with regard to a potential interaction of rufinamide on phenythoin clearance. The information were only mentioned in the CCDS. The MAH was requested to argue the reason of the missing data in the EU SmPC. As a consequence three different analysis were submitted by the MAH. Although result from the initial analysis showed a small effect on rufinamide on the clearance of phenytoin, two additional sub-sequent analysis demonstrated that rufinamide appears not to have a clinically relevant effect on phenytoin concentration. This information has been clearly mentioned in Section 4.5 of the tablets SmPC, in line with the information already included in the oral supsension.

IA/0024	B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place	28/08/2012	n/a		
IB/0021	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	11/05/2012	n/a		
IA/0022/G	This was an application for a group of variations. 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) 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) 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) A.7 - Administrative change - Deletion of manufacturing sites	04/04/2012	n/a		
R/0020	Renewal of the marketing authorisation.	17/11/2011	09/01/2012	SmPC and PL	Based on the review of the available information, the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and

					sufficiently demonstrated and therefore considers the benefit/risk profile of Inovelon continues to be favourable. Following the introduction of the new oral formulation, the MAH should continue to submit yearly PSURs. The CHMP is also of the opinion that the renewal can be granted with unlimited validity.
X/0017	Annex I_2.(d) Change or addition of a new pharmaceutical form Annex I_2.(c) Change or addition of a new strength/potency	22/09/2011	21/11/2011	SmPC, Annex II, Labelling and PL	
N/0019	The Marketing Authorisation Holder (MAH) took the opportunity to update details of local representatives in Annex IIIB Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/03/2011	n/a	PL	
IA/0018/G	This was an application for a group of variations. B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions B.II.a.3.b.1 - Changes in the composition (excipients) of the finished product - Other excipients - Any minor adjustment of the quantitative composition of the finished product with respect to excipients	06/01/2011	n/a		

IB/0016	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	07/09/2010	n/a		
IB/0015	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	23/10/2009	n/a	SmPC	
IA/0014	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	05/08/2009	n/a		
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/08/2009	n/a	PL	
IA/0012	IA_01_Change in the name and/or address of the marketing authorisation holder	10/03/2009	n/a	SmPC, Labelling and PL	
IA/0011	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	10/02/2009	n/a	Annex II and PL	
N/0010	Update of the list of local representatives in section 6 of the Package Leaflet; correction of minor linguistic changes in the English and Portuguese PL and correction to the Hungarian term for tablet in the labelling.	14/01/2009	n/a	Labelling and PL	

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IA/0009	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	02/07/2008	n/a		
II/0007	Update of section 4.2 of the Summary of Product Characteristics in relation to the dosing regimen for patients under 30 kg also taking valproate medication. Update of Summary of Product Characteristics and Package Leaflet	19/03/2008	08/04/2008	SmPC and PL	As valproate significantly decreases clearance of Inovelon, a lower maximum dose of Inovelon is recommended for patients under 30 kg also taking valproate medication. Therefore, if doctors prescribe or recommend an additional treatment for epilepsy (e.g. valproate) patient must tell them that they are taking Inovelon. Their dose may then need adjusting. In particular, following the evaluation of additional studies for children under 30 kg also receiving valproate treatment, the maximum recommended daily dose was increased from 400 to 600 mg/day.
IA/0008	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	28/02/2008	n/a		
IA/0006	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	18/01/2008	n/a		
IA/0005	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	18/01/2008	n/a	Annex II and PL	
II/0003	Update of section 4.4 of the Summary of Product Characteristics with information on the findings of	19/07/2007	23/08/2007	SmPC	The MAH performed a QTc study to evaluate the effect of inovelon compared to that of placebo on ventricular

	the QTc study E2080-A001-002, which showed that inovelon produced a decrease in QTc interval. Update of Summary of Product Characteristics				repolarization in healthy subjects. The study showed that rufinamide produced a decrease in QTc interval proportional to concentration. Although the underlying mechanism and relevance of this finding is not known, the CHMP recommended clinicians to use their clinical judgment when assessing whether to prescribe rufinamide to patients at risk from further shortening their QTc duration (eg. Congenital short QT syndrome or patients with a family history of such a syndrome)".
IA/0004	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	09/07/2007	n/a		
IB/0002	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	11/05/2007	n/a		
IB/0001	IB_10_Minor change in the manufacturing process of the active substance	11/05/2007	n/a		