Ameluz

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/0055	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/12/2023		SmPC and PL	
IB/0057/G	This was an application for a group of variations.	04/12/2023		SmPC, Labelling and	

[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).

	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.a.3.z - Changes in the composition (excipients) of the finished product - Other variation B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)			PL	
IB/0056	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	28/04/2023	n/a		
IA/0054/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	08/11/2022	n/a		

	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				
II/0049/G	This was an application for a group of variations. B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF B.I.b.1.i - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Where there is no monograph in the European/National Ph. for the AS, a change in specification from in-house to a non-official/third country Ph. A.7 - Administrative change - Deletion of manufacturing sites	06/10/2022	n/a		
IB/0053/G	This was an application for a group of variations. 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 B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS	09/09/2022	n/a		

N/0052	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/03/2022		Labelling and PL	
PSUSA/10006 /202106	Periodic Safety Update EU Single assessment - 5-aminolevulinic acid (keratosis)	10/02/2022	n/a		PRAC Recommendation - maintenance
IB/0051/G	This was an application for a group of variations. 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.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	07/01/2022	n/a		
IB/0048/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol A.7 - Administrative change - Deletion of manufacturing sites B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS B.I.a.3.d - Change in batch size (including batch size ranges) of AS or intermediate - More than 10-fold increase compared to the originally approved batch	10/09/2021	n/a		

	size 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.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0046/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	18/03/2021	n/a		
N/0047	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/03/2021	10/02/2022	PL	
IB/0045/G	This was an application for a group of variations.	19/02/2021	10/02/2022	SmPC	

	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.e.2.d - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition or replacement of a specification parameter as a result of a safety or quality issue B.II.e.2.d - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition or replacement of a specification parameter as a result of a safety or quality issue 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) B.II.e.z - Change in container closure system of the Finished Product - Other variation B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation				
IB/0044/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch	12/11/2020	n/a		

	size				
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/08/2020	10/02/2022	PL	
IB/0042	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	15/07/2020	n/a		
II/0040	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	12/03/2020	n/a		
II/0039/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	30/01/2020	09/03/2020	SmPC and PL	Please refer to Scientific Discussion 'Ameluz-H-C-2204-II-0039'
IB/0041/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished	27/01/2020	n/a		

	product - Other changes to a test procedure (including replacement or addition)				
IB/0038	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	04/09/2019	n/a		
IB/0037/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.b.z - Change in control of the AS - Other variation	29/05/2019	n/a		
PSUSA/10006 /201806	Periodic Safety Update EU Single assessment - 5-aminolevulinic acid (keratosis)	28/02/2019	26/04/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10006/201806.
IB/0033/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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	19/12/2018	n/a		

	B.I.b.z - Change in control of the AS - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol				
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/12/2018	26/04/2019	Labelling and PL	
IB/0031/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation 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 originally approved batch size	08/10/2018	n/a		
IA/0035	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)	21/09/2018	n/a		
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/07/2018	26/04/2019	PL	
IA/0029/G	This was an application for a group of variations. B.II.c.2.a - Change in test procedure for an excipient	19/04/2018	n/a		

	- Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure				
II/0027/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.5.b - Change in the legal status of a medicinal product for centrally authorised products - All other legal status changes	25/01/2018	01/03/2018	SmPC, Annex II and PL	
IA/0028/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	27/10/2017	n/a		
IB/0026/G	This was an application for a group of variations. 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 B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished	12/04/2017	n/a		

	product - Other variation B.II.d.1.g - Change in the specification parameters and/or limits of the finished product - Addition or replacement (excluding biological or immunological product) of a specification parameter wit its corresponding test method as a result of a safety or quality issue				
II/0024	Extension of Indication from "Treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2; see section 5.1) and of field cancerization" to the following: Treatment of superficial and/or nodular basal cell carcinoma unsuitable for surgical treatment due to possible treatment-related morbidity and/or poor cosmetic outcome in adults. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. Editorial changes have been proposed in sections 4.2, 4.4, 5.2, 6.6 and 9 of the SmPC. The Package Leaflet and Labelling are updated accordingly. There are two new warnings that have been included in section 4.4 that the use of immunosuppressants during treatment with Ameluz is not recommended and of the risk of transient global amnesia. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10. The variation leads to amendments to the Summary of Product Characteristics, Package Leaflet and to the	15/12/2016	27/01/2017	SmPC, Annex II, Labelling and PL	Please refer to the published Assessment Report Ameluz H-2204-II-24-AR.

	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				
IA/0025	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	16/12/2016	n/a		
R/0023	Renewal of the marketing authorisation.	15/09/2016	21/11/2016	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Ameluz in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0020	Extension of Indication to include treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerization based on the phase III clinical study ALA-AK-CT007. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet and to bring section 6.6 of the SmPC in line with the latest QRD template. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	21/07/2016	09/09/2016	SmPC and PL	Please refer to the published assessment report Ameluz-H-C-2204-II-0020-AR.

IB/0021/G	This was an application for a group of variations. B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale B.II.f.1.e - Stability of FP - Change to an approved stability protocol	31/03/2016	09/09/2016	SmPC	
IA/0022/G	This was an application for a group of variations. B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	23/03/2016	n/a		
PSUSA/10006 /201506	Periodic Safety Update EU Single assessment - 5-aminolevulinic acid (keratosis)	14/01/2016	n/a		PRAC Recommendation - maintenance
IB/0018/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF 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	09/12/2015	n/a		

	B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation				
IB/0019	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	02/12/2015	n/a		
IAIN/0016/G	This was an application for a group of variations. 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 C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) in the safety database and/or major contractual arrangements for the fulfilment of PhV obligations, and/or change of the site undergoing PhV activities	18/06/2015	n/a		
IAIN/0015/G	This was an application for a group of variations. 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.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/04/2015	n/a		

II/0012	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	26/03/2015	n/a		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/01/2015	09/09/2016	PL	
II/0011	To change the manufacturer of the active substance and to change the site where testing is performed. B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	22/01/2015	n/a		
PSUSA/10006 /201406	Periodic Safety Update EU Single assessment - 5-aminolevulinic acid (keratosis)	09/01/2015		SmPC and PL	PRAC Recommendation - maintenance
IB/0010/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	24/02/2014	n/a		

PSUSA/10006 /201306	Periodic Safety Update EU Single assessment - 5-aminolevulinic acid (keratosis)	23/01/2014	n/a		PRAC Recommendation - maintenance
N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/12/2013	17/01/2014	PL	
IA/0007/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/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size	16/12/2013	n/a		
IB/0006/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	17/10/2013	n/a		
N/0005	The MAH applied to update the list of local representatives: CZ, HU, SI and SK have now a local representative other than Biofrontera Pharma GmbH.	23/05/2013	17/01/2014	PL	

	In addition, the contact details for SE has been changed. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IB/0004	B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	10/01/2013	n/a		
IB/0003/G	This was an application for a group of variations. 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) B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data) B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	04/01/2013	17/01/2014	SmPC, Labelling and PL	
IA/0002/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	16/11/2012	n/a		

	product, including quality control sites (excluding manufacturer for batch release) B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
N/0001	The Marketing authorisation Holder added the List of local representatives to the Package Leaflet. Furthermore minor linguistic and editorial amendments to the Labelling and Package Leaflet were made for BG, CS, DA, DE, EL, ES, ET, FI, FR, IS, IT, LV, MT, NL, No, PL, PT, RO, SK, SL, SV. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/08/2012	17/01/2014	Labelling and PL	