Lumigan

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
IB/0067	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/11/2024		SmPC, Labelling and PL	
N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/07/2022		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).

T/0065	Transfer of Marketing Authorisation	29/04/2022	13/05/2022	SmPC, Labelling and PL	
PSUSA/413/202103	Periodic Safety Update EU Single assessment - bimatoprost	11/11/2021	20/01/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/413/202103.
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/06/2021	20/01/2022	PL	
N/0062	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/02/2021	21/04/2021	PL	
IA/0061	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	02/10/2020	n/a		
IB/0060	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	04/05/2020	21/04/2021	Annex II and PL	
IB/0059	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	17/02/2020	n/a		
N/0058	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/03/2019	21/04/2021	PL	
PSUSA/413/201803	Periodic Safety Update EU Single assessment - bimatoprost	15/11/2018	18/01/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/413/201803.

IB/0057	B.II.e.z - Change in container closure system of the Finished Product - Other variation	04/09/2018	18/01/2019	SmPC, Labelling and PL	
II/0055	Submission of the final report of the Phase 4 clinical safety study P-192024-054 to evaluate the long-term safety of Lumigan 0.1 mg/ml compared with Lumigan 0.3 mg/ml and listed as a category 3 study in the RMP. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/04/2018	n/a		
WS/1084/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.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 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	14/09/2017	n/a		

II/0052	Update of the Lumigan 0.1 mg/ml eye drops SmPC section 4.8 to add the adverse reactions Eye discharge, Lacrimation increased, Eye oedema and Foreign body sensation in eyes in line with the Company Core Data Sheet. The Package Leaflet has been updated accordingly. Section 3 of the PL was also amended to improve clarity of instructions. In addition, the MAH took the opportunity to update the Product Information in line with the QRD template version 10 and implement the unique identifier 2D barcode. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/05/2017	12/04/2018	SmPC, Annex II, Labelling and PL	
IB/0051	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	24/06/2016	n/a		
N/0050	Update of the package leaflet with revised contact details of the local representatives for Bulgaria, Czech Republic, Germany, Estonia, Greece, Cyprus, Spain, Iceland, Latvia, Lithuania, Hungary, Austria, Romania, and Slovak Republic. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/03/2016	12/04/2018	PL	
PSUSA/413/201503	Periodic Safety Update EU Single assessment - bimatoprost	19/11/2015	14/01/2016	SmPC and PL	Please refer to Lumigan PSUSA-00000413-201503 EPAR: Scientific conclusions and grounds recommending the

					variation to the terms of the marketing authorisation
IAIN/0048	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	21/05/2015	n/a		
N/0047	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/08/2014	14/01/2016	PL	
PSUV/0046	Periodic Safety Update	24/10/2013	20/12/2013	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0046.
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.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling	15/11/2013	n/a		

	down to 10-fold 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.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 or intermediate product - Other variation				
IA/0044/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) 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)	17/10/2013	n/a		

II/0042	Update of sections 4.3, 4.4 and 4.8 of the SmPC mainly in order to strengthen the existing warning on avoiding allowing the tip of the dispensing container to contact the eye. The Package Leaflet was updated accordingly. Additionally, the CHMP-recommended text for phosphate-containing eye drops has been included in the SmPC and PL. Furthermore, the PI is being brought in line with the latest QRD template version 9. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	19/09/2013	20/12/2013	SmPC, Annex II, Labelling and PL	The safety information in the SmPC for Lumigan was updated, to provide the most up to date safety guidance for Lumigan multi-dose eye drops solution, in order to prevent eye injuries while using the product. Additionally, text has been added to inform that, as for other eye drops containing phosphates, in very rare cases, some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment.
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/07/2013	20/12/2013	PL	
IB/0041	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	21/03/2013	20/12/2013	SmPC, Labelling and PL	
T/0040	Transfer of Marketing Authorisation	05/02/2013	25/02/2013		
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/02/2013	20/12/2013	Labelling and PL	
II/0036/G	This was an application for a group of variations. To introduce two new presentations: two preservative free formulations of Lumigan 0.3 mg/ml, eye-drops, solution, in single-dose container	18/10/2012	19/11/2012	SmPC, Labelling and PL	

	(pack sizes 5 and 30) B.II.a.3.b.2 - Changes in the composition (excipients) of the finished product - Other excipients - Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the product B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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.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 B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range 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.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes				

	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
IAIN/0037	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	31/10/2012	n/a		
II/0035	Update of sections 4.4, 4.5 and 4.8 of the Summary of Product Characteristics (SmPC) to include information in the SmPC for both Lumigan 0.1 mg/ml and 0.3 mg/ml in line with the recently amended Company Core Data Sheet and provide prescribers with up to date safety guidance. Sections 2, 3 and 4 of the Package Leaflet were updated accordingly. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/06/2012	23/07/2012	SmPC, Annex II, Labelling and PL	The following updates of the Summary of product characteristics (SmPC) were considered relevant by the CHMP: 4.4 Special Warnings and Precautions section of the SmPC: - Addition of more information on darker iris colour - Addition of hair growth precaution - Addition of information on the consequences of more frequent than once a day administration - Addition of information relating to bacterial keratitis with multidose containers 4.5 Interactions with other medicinal products section - Addition of information on concomitant use of Lumigan with other prostaglandin analogues 4.8 Undesirable effects section - 'eye pain' was added as common side effect with Lumigan 0.1 mg/ml - 'periorbital erythema' as uncommon side effect with Lumigan 0.3 mg/ml

					- 'blurred vision' was added to the list of common side effects for Lumigan 0.3 mg/ml - 'pigmentation of periocular skin' was removed from table 2 in Lumigan 0.01% as it was redundant. The Package Leaflet was updated accordingly.
N/0034	The Marketing Authorisation Holder (MAH) took the opportunity to update details of local representatives in Annex IIIB. Furthermore, Annex IIB was updated by deleting the DDPS version number. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/07/2011	n/a	Annex II and PL	
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/01/2011	n/a	PL	
II/0031	Introduction of a new active substance manufacturer B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is supported by an ASMF	16/12/2010	04/01/2011		
IA/0032	A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	26/11/2010	n/a		
II/0030	Change in the control process for the finished product.	18/03/2010	24/03/2010		

	Quality changes				
II/0029	Inclusion of alternative packaging suppliers for Lumigan 0.03%. Quality changes	18/02/2010	25/02/2010		
X/0026	Change or addition of a new strength/potency. Annex I_2.(c) Change or addition of a new strength/potency	22/10/2009	07/01/2010	SmPC, Annex II, Labelling and PL	The MAH applied for a new strength (Lumigan 0.1 mg/ml eye drops, solution) to provide a therapeutic alternative to the other approved formulation (0.3 mg/ml). The product line will now have two options, one with a reduced concentration of bimatoprost or one with a low benzalkonium chloride concentration. Choice between two formulations will depend on the patient's ocular status and ability to tolerate the product. The new presentation is aimed at improving the ocular surface tolerability, mainly conjunctival hyperaemia (redness of the eye), by reducing to one third the content of bimatoprost (i.e. from 0.03% to 0.01%). This leads to a 4-fold increase of the preservative BAK in order to achieve a greater absorption of the active substance. The CHMP considered the benefits of Lumigan 0.01 % formulation outweigh the potential risks.
II/0028	Update of Summary of Product Characteristics and Package Leaflet , mainly to update Section 4.8 of the SPC based on a recent update of the MAH's Core Data Sheet.	23/07/2009	02/09/2009	SmPC and PL	The rationale in support of the changes was based on a cumulative safety analysis of adverse events (collected up to 31 August 2008) as part of a revision of the Company Core Data Sheet for Lumigan. The review provided by the MAH was considered to be adequate and the MAH proposals

	Update of Summary of Product Characteristics and Package Leaflet				were endorsed. The following two adverse events have been included: 'Nausea' and 'enophthalmos'. The following three adverse events have been deleted: 'Peripheral oedema', 'infection' (primarily colds and upper respiratory infections), and 'cataract'. In addition, aspects of section 4.4 concerning iris and periorbital tissue pigmentation have been updated. The recommendations on lactation in section 4.6 were also updated in line with the recommendations of the Guideline on risk assessment of medicinal products on human reproduction and lactation.
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/02/2009	n/a	PL	
II/0024	Change(s) to the test method(s) and/or specifications for the finished product	19/03/2008	28/03/2008		
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/03/2008	n/a	Labelling and PL	
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2007	n/a	Labelling and PL	
IB/0022	IB_33_Minor change in the manufacture of the finished product	25/05/2007	n/a		
IA/0021	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	27/02/2007	n/a		
R/0020	Renewal of the marketing authorisation.	14/12/2006	20/02/2007	SmPC, Labelling and	Based on their review of the available information and on the basis of a re-evaluation of the benefit risk balance, the

				PL	CHMP was of the opinion that the quality, safety and efficacy continue to be adequately and sufficiently demonstrated. Therefore, the benefit/risk profile of Lumigan continues to be favourable. The CHMP recommended the renewal of the Marketing Authorisation for Lumigan with unlimited validity.
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2006	n/a	PL	
IB/0018	IB_33_Minor change in the manufacture of the finished product	31/07/2006	n/a		
II/0017	Update of Summary of Product Characteristics (section 4.8, Undesirable effects and section 4.4 Special Warnings and Special Precautions for Use) Update of Summary of Product Characteristics	23/03/2006	27/04/2006	SmPC	Further to their conclusions of the assessment of PSURs 4 and 5, the CHMP requested a variation to change the term "Elevated liver function" to the term "liver function test abnormal" and to amend the frequency grouping in section 4.8 (Undesirable effects) of the SPC, in accordance with the current Guideline on SPC.
IB/0016	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening IB_37_a_Change in the specification of the finished product - tightening of specification limits	13/12/2004	n/a		
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/07/2004	n/a	PL	
IA/0015	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	24/06/2004	n/a		
IA/0014	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	24/06/2004	n/a		

N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/05/2004	n/a		
II/0008	Extension of Indication Update of Summary of Product Characteristics and Package Leaflet	22/10/2003	20/01/2004	SmPC and PL	
IA/0011	IA_28_Change in any part of primary packaging material not in contact with finished product	05/11/2003	n/a		
I/0010	31_Change in container shape	05/08/2003	22/09/2003		
I/0009	25_Change in test procedures of the medicinal product	16/06/2003	17/06/2003		
I/0007	15_Minor changes in manufacture of the medicinal product	08/04/2003	08/04/2003		
I/0006	03_Change in the name and/or address of the marketing authorisation holder 01_Change in the name of a manufacturer of the medicinal product	01/10/2002	23/10/2002	SmPC, Labelling and PL	
I/0005	01_Withdrawal of the manufacturing authorisation for a site of manufacture	01/10/2002	07/10/2002		
I/0001	30_Change in pack size for a medicinal product	17/05/2002	09/07/2002	SmPC, Annex II, Labelling and PL	
I/0004	23_Change in storage conditions	17/05/2002	27/05/2002		

I/0003	31_Change in container shape	17/05/2002	27/05/2002		
I/0002	15_Minor changes in manufacture of the medicinal product	17/05/2002	27/05/2002		