Travatan

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
IAIN/0067/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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	29/09/2021		Annex II and 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).

	including batch control/testing 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				
IA/0066	B.II.c.4.a - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Minor change	17/03/2021	n/a		
WS/1944	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	26/11/2020	n/a		
IAIN/0065/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	30/09/2020	n/a		
IB/0062/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	16/04/2020	n/a		
IB/0063	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	13/03/2020	n/a		

PSUSA/3011/ 201902	Periodic Safety Update EU Single assessment - travoprost	31/10/2019	n/a		PRAC Recommendation - maintenance
IA/0060	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	03/08/2018	09/08/2019	SmPC, Annex II, Labelling and PL	
WS/1385	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	26/07/2018	09/08/2019	SmPC	
T/0059	Transfer of Marketing Authorisation	16/04/2018	08/05/2018	SmPC, Labelling and PL	
II/0057	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	23/11/2017	n/a		
II/0053	Following the submission of final CSR for study C-01-79 and a review of supporting clinical studies and post-marketing data, update to SmPC section 4.8 is proposed. The package leaflet is updated accordingly. In addition, MAH took the opportunity to update number of the Spanish representative in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/04/2017	13/04/2018	SmPC and PL	The section 4.8 of SmPC has been updated with four new adverse events based on post-marketing data: insomnia, arrhythmia, epistaxis and vomiting with frequency unknown. In addition, section 4.8 of SmPC has been updated following review of clinical trials data as follows: cough frequency has been upgraded from rare to uncommon and arthralgia frequency has been upgraded from not known to rare; dizziness, asthenopia,

					dyspnoea, asthma, visual field defect have been downgraded to frequency rare; and four adverse reactions were included: trichiasis, eyelash hyperpigmentation (recoded from eyelash discoloration, frequency downgraded), rhinitis allergic, nasal dryness (based on several nasal disorders already listed) and ophthalmic herpes simplex (recoded from the combination with herpes simplex and keratitis herpetic). For further details see the Annexes. The Patient Information Leaflet has been updated accordingly.
T/0056	Transfer of Marketing Authorisation	06/04/2017	20/04/2017	SmPC, Labelling and PL	
IB/0055/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 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	01/03/2017	n/a		

	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.II.c.4.a - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Minor change				
IB/0054	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	17/02/2017	n/a		
PSUSA/3011/ 201602	Periodic Safety Update EU Single assessment - travoprost	29/09/2016	n/a		PRAC Recommendation - maintenance
PSUSA/3011/ 201502	Periodic Safety Update EU Single assessment - travoprost	08/10/2015	n/a		PRAC Recommendation - maintenance
IAIN/0050	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	26/03/2015	25/01/2016	SmPC and Labelling	
II/0049/G	This was an application for a group of variations. B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	22/01/2015	25/01/2016	SmPC, Labelling and PL	
II/0046	Extension of the therapeutic indication for the decrease of elevated intraocular pressure in paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated.	20/11/2014	19/12/2014	SmPC and PL	Please refer to Scientific Discussion Travatan-H-390-II-46-AR.

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/3011/ 201402	Periodic Safety Update EU Single assessment - travoprost	09/10/2014	n/a		PRAC Recommendation - maintenance
IG/0452	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	28/07/2014	n/a		
II/0044	Update of sections 4.2, 4.4, 4.6, 4.7 and 4.8 of the SmPC following a review of the available clinical and post-marketing data. The Package Leaflet and Labelling 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	25/04/2014	19/12/2014	SmPC, Annex II, Labelling and PL	The MAH undertook a review of the available data supporting the safety profile of Travatan 40 micrograms/ml eye drops. No new clinical trial data were evaluated for the purpose of this review, which was based on data from previously completed clinical studies and post-marketing experience with the product. Practical instructions about the tamper evident snap collar were also included ("After the cap is removed, if the tamper evident snap collar is loose, remove before using product").
IG/0324	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/07/2013	n/a		
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/07/2013	31/01/2014	PL	
IG/0274	A.1 - Administrative change - Change in the name and/or address of the MAH	19/03/2013	31/01/2014	SmPC, Labelling and PL	

II/0039	Update of the side effects sections of the SmPC and PL as recommended by the CHMP, to add 'sunken eyes' to the list of observed side effects. 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	17/01/2013	31/01/2014	SmPC and PL	During a post-marketing review of the safety of Travatan, "sunken eyes" was identified as an additional risk associated with the class of medicines Travatan belongs to (i.e. prostaglandin analogues). For this reason, the CHMP requested to update the production information accordingly. With this variation, the term "sunken eyes" was added to the SmPC and PL for Travatan.
IB/0038/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	18/09/2012	n/a		
IB/0037	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	12/05/2011	n/a		
II/0036	Update of Summary of Product Characteristics based on a recommendation from the CHMP contained in the conclusions of a previous procedure (EMEA/H/C/390/II/032). C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/03/2011	14/04/2011	SmPC	Section 4.8 of the Travatan SPC has been revised based on a request from the CHMP contained in the conclusions of procedure EMEA/H/C/390/II/032. With this variation, the System Organ Classification "Eye Disorders" within the tables of ADRs is section 4.8 of the

					Travatan SPC is now described more clearly, focusing on the most substantial information. No new safety information has been added to the revised SPC.
II/0035/G	This was an application for a group of variations. To change the preservative in the finished product. To introduce manufacturing overage for the active substance. To add a new test method in the finished product specification. To reduce in the shelf-life of the finished product. To change the release and shelf-life specification of the finished product. To change the active substance assay method for the finished product. 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.3.e - Change in the manufacturing process of the finished product - Introduction or increase in the overage that is used for the AS 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 as a result of a safety or quality issue B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	21/10/2010	29/11/2010	SmPC, Annex II, Labelling and PL	

II/0032	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	23/09/2010	28/10/2010	SmPC and PL	Subsequent to the approval of the first line indication for Travatan (EMEA/H/C/390/II/06), Alcon committed to complete a long-term clinical study (C-02-20, of a 5-year duration). The Report for this study was completed and submitted in December 2009 (FUM 023). The CHMP assessment of the Report was completed in March 2010, and concluded that no safety issues of concern resulted from this study. In the light of the new available data on safety, the MAH reviewed the SPC to update section 4.8 with the information emerging from the completion and assessment of study C-02-20. As result of this update, the occurrence of the term 'iris hyperpigmentation' was changed to the 'very common' range. Several new Adverse Drug Reactions were added to the SPC with frequency categorised as uncommon. The PL text was also updated to be in line with the SPC.
IA/0034	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	04/06/2010	n/a		
IA/0033	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	04/06/2010	n/a		

IB/0031	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	07/04/2010	n/a		
II/0030	To add an alternate site of manufacture for travoprost. Quality changes	17/12/2009	07/01/2010		
II/0029	To increase of the number of holding days during the filling process of Travatan 40 micrograms/ml Eye Drops, Solution. Quality changes	24/09/2009	05/10/2009		
IB/0028	IB_14_b_Change in manuf. of active substance without Ph. Eur. certificate - new manufacturer	19/02/2009	n/a		
IB/0027	IB_14_b_Change in manuf. of active substance without Ph. Eur. certificate - new manufacturer	19/02/2009	n/a		
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/01/2009	n/a	Labelling and PL	
IA/0025	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	06/10/2008	n/a		
IB/0024	IB_36_a_Change in shape or dimensions of the container/closure - sterile ph. forms/biologicals	30/09/2008	n/a		
IB/0023	IB_36_a_Change in shape or dimensions of the container/closure - sterile ph. forms/biologicals	29/09/2008	n/a		

IB/0021	IB_10_Minor change in the manufacturing process of the active substance	12/12/2007	n/a		
II/0020	Change to the site for ethylene oxide sterilisation of the primary packaging for Travatan eye drops. Quality changes	15/11/2007	21/11/2007		
II/0017	Update of Summary of Product Characteristics and Package Leaflet. Update of Summary of Product Characteristics and Package Leaflet	24/01/2007	01/03/2007	SmPC, Annex II and PL	Further to the conclusions of the procedure for Renewal of the Marketing Authorisation, as recommended by CHMP, the Marketing Authorisation Holder (MAH) applied for an update of section 4.8 of the Summary of Product Characteristic (SPC) to be in accordance with MedDRA SOCs classification and order. Additionally, the frequency of several adverse reactions has been updated and new adverse reactions obtained from completed and ongoing studies have been added. The Package Leaflet was amended accordingly.
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/01/2007	n/a	PL	
IB/0018	IB_14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	06/12/2006	n/a		
R/0016	Renewal of the marketing authorisation.	27/07/2006	06/10/2006	SmPC, Labelling and	Based on their review of the available information and on the basis of a re-

				PL	evaluation of the benefit risk balance, the CHMP was of the opinion that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considered that the benefit/risk profile of Travatan continues to be favourable. The CHMP recommended the renewal of the Marketing Authorisation for Travatan. The CHMP was also of the opinion that the renewal can be granted with unlimited validity. The renewal required amendments to the following annexes have been amended: SPC, Labelling and Package Leaflet.
IB/0015	IB_10_Minor change in the manufacturing process of the active substance	25/04/2006	n/a		
IB/0014	IB_10_Minor change in the manufacturing process of the active substance	05/01/2006	n/a		
II/0013	Change(s) to the manufacturing process for the finished product	15/12/2004	25/01/2005	Annex II and PL	
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/11/2004	n/a	PL	
N/0010	MAH applied for the inclusio of additional local representatives of the MAH for all new Members States and of an electronic contact address for the Swedish local representative.	13/05/2004	n/a	PL	

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
II/0009	Update of Summary of Product Characteristics and Package Leaflet	24/07/2003	24/10/2003	SmPC and PL	
II/0006	Update of Summary of Product Characteristics and Package Leaflet	25/04/2003	28/07/2003	SmPC and PL	
I/0008	11a_Change in the name of a manufacturer of the active substance	19/05/2003	26/05/2003		
I/0007	20_Extension of shelf-life as foreseen at time of authorisation	10/01/2003	14/02/2003	SmPC	
II/0005	Update of Summary of Product Characteristics and Package Leaflet	22/08/2002	12/11/2002	SmPC and PL	
I/0004	11_Change in or addition of manufacturer(s) of active substance	17/07/2002	24/07/2002		
I/0003	14_Change in specifications of active substance	27/06/2002	05/07/2002		
I/0001	11_Change in or addition of manufacturer(s) of active substance	07/02/2002	15/02/2002		
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/02/2002	14/03/2002	PL	