Ganfort

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/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/03/2019		PL	
IB/0030	B.II.e.z - Change in container closure system of the Finished Product - Other variation	18/10/2018		SmPC, Labelling and PL	
WS/1084/G	This was an application for a group of variations following a worksharing procedure according to Article	14/09/2017	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).

	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				
II/0026	Update of section 4.8 as per the PRAC recommendation following the PSUSA assessment. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the Product Information in line with the QRD template version 10.0, implement the unique identifier – 2D bar code and correct typographical errors. As per the PRAC recommendation, the updated RMP version 3.2 is also agreed. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	06/04/2017	27/03/2018	SmPC, Annex II, Labelling and PL	As per the recommendation following the PSUSA assessment (EMEA/H/C/PSUSA/00002961/201511), section 4.8 of the Ganfort SmPC is being updated to improve clarity, consistency and readability as well as to implement the Lumigan PSUR recommendation regarding ADRs pertaining to bimatoprost (addition of asthma exacerbation and COPD exacerbation). The Package Leaflet is updated accordingly.
PSUSA/2961/ 201511	Periodic Safety Update EU Single assessment - bimatoprost / timolol	21/07/2016	15/09/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/2961/201511.
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/02/2016	15/09/2016	PL	
IAIN/0023	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	12/06/2015	n/a		
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/09/2014	15/09/2016	PL	
IA/0021/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)	28/10/2013	n/a		
PSUV/0020	Periodic Safety Update	25/07/2013	04/10/2013		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0020.
II/0019	Update of sections 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information in line with their latest Company Core Safety Information (CCSI) document. Section 4 of the Package Leaflet was updated accordingly.	30/05/2013	04/10/2013	SmPC, Annex II and PL	To reflect a safety review carried out by the MAH, which led to update of the Company's position on the safety of Ganfort, with this variation, the MAH proposed to change the prescribing and patient information in relation to the active substances bimatoprost and timolol.

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				The CHMP considered the proposals for the SmPC sections 4.4, 4.8 and 4.9, and PL section 4 to be acceptable and overall improve the text of the prescribing and patient information. The main changes were addition of clarifying text in the warnings section to describe possible reasons for changes to the colour of the iris. Warnings on the use of Ganfort during active eye inflammation, potential for hair growth and potential consequences of taking more than one bimatoprost dose per day were also included. Additionally, section 4.8 was revised, mainly to update the frequencies of some side effects.
II/0017/G	This was an application for a group of variations. To introduce a new preservative free 0.4 ml presentation of Ganfort 0.3 mg/ml eye-drops solution, in single-dose container. As a consequence, the product formulation, specification and test methods were updated, and a new supplier of the container closure system for the new preservative free presentations was introduced. The new presentation is available in packs of 5, 30 and 90 containers. 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.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	30/05/2013	04/10/2013	SmPC, Labelling and PL	

	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.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				
T/0018	Transfer of Marketing Authorisation	07/02/2013	13/03/2013		
IAIN/0016	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	31/10/2012	n/a		
II/0015	Removal of the restriction to morning-only dosing from the posology section (4.2) of the SPC in order to allow a choice of either morning or evening once-daily dosing. The pharmacodynamics section (5.1) of the SPC has also being updated regarding morning and evening posology. The Package Leaflet (PL) has also been revised in line with the SPC wording.	20/09/2012	24/10/2012	SmPC and PL	This change to the dosing regimen recommendations from morning dosing to the possibility of morning or evening dosing of Ganfort eye drops was supported by a comprehensive review of two GCP compliant studies published in peer reviewed journals. One directly compares am to pm dosing of Ganfort eye drops in exfoliative glaucoma patients, the other comparing the IOP decreasing effect of Ganfort and a travoprost/timolol fixed combination eye

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				drops, both dosed in the evening. A literature review of supportive studies and a justification of the extrapolation of the patient population with exfoliative glaucoma to a population with open angle glaucoma are also major parts of the submission. The MAH has demonstrated that the proposed amendment to SPC Section 4.2 is appropriate. The safety information from the pm dosing regimen is consistent with what is known from the am dosing schedule – with the reservation that literature data do not possess the same accuracy than data collected in clinical trials with regulatory purpose. There is, however, no reason to believe that a pm dosing should be more prone to adverse events – on the contrary, a slightly better outcome may be anticipated as some adverse events may occur during sleep, thus being less bothersome to the patient. Compliance may be a weak point in glaucoma patients, who in earlier stages are symptom free and hence not always adhering to the prescriptions. Hence, any potential benefit of compliance might improve the outcome for patients with this often symptom-free disorder. In conclusion, the proposed changes in sections 4.2 and 5.1 in the Ganfort SPC do not have any impact on the positive Benefit / Risk Balance of Ganfort eye drops.
II/0014	Update of section 4.8 of the SPC ('Undesirable effects') in order to update the safety information to include three new effects: Iris hyper-pigmentation, deepening of the eyelid sulcus and periocular skin hyper-pigmentation. The Package Leaflet is updated accordingly.	20/09/2012	24/10/2012	SmPC, Annex II, Labelling and PL	Following a review of the safety data available for Ganfort, "periocular skin hyper-pigmentation" (darker skin colour around the eyes) was added to the list of side effects observed while using Ganfort with a frequency 'common'. "Iris hyper-pigmentation" (darker iris colour) and "deepening of the eyelid sulcus" (eyes appearing sunken"

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				were also added to the list of side effects, with 'uncommon' frequency.
IB/0013	C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH	15/12/2011	06/07/2012	SmPC and PL	Update of the Summary of Product Characteristics to add the agreed PhVWP class wording for beta-blockers class. In section 4.8 Undesired Effects, only additional adverse events associated with the beta-blocker monotherapy (and not seen with Ganfort fixed-dose combination) have been listed for timolol. The Package Leaflet has also been revised to bring in line with the recommended PhVWP PL wording and the proposed SPC. The recommended PhWVP PL wording was amended slightly in some parts to make the wording more patient friendly.
IA/0012	B.III.1.a.3 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	28/06/2011	n/a		
R/0011	Renewal of the marketing authorisation.	14/04/2011	23/06/2011	SmPC, Labelling and PL	The benefit/risk for the product was assessed based on the submitted PSUR data and safety/efficacy data accumulated since the granting of the MA and a review of literature data. No new pre-clinical or clinical data were available which changed or resulted in a changed risk-benefit evaluation. Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP was of the opinion that the quality, safety and efficacy of Ganfort continued to be adequately and sufficiently demonstrated and therefore considered that the benefit risk profile of Ganfort continues to be favourable. The CHMP was also of the opinion that the renewal could be granted with

					unlimited validity.
II/0008	Introduction of a new manufacturer of the active substance that is supported by an ASMF. 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	03/01/2011		
IA/0010	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	30/11/2010	n/a		
N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/07/2010	n/a	PL	
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/01/2010	n/a	PL	
II/0006	Changes to the registered parameters of the sterilisation cycle for the container closure system due to operational reasons. The opportunity was also taken to consolidate the set of registered parameters . Change(s) to the manufacturing process for the finished product	24/09/2009	29/09/2009		
II/0005	Further to the CHMP conclusions after assessment of PSUR 4, updates of sections 4.4 (Special warnings and precautions for use) and section 4.8 of the Summary	22/01/2009	02/03/2009	SmPC and PL	Following assessment of PSUR 4 for Ganfort, the CHMP recommended amendments to section 4.4 of the SPC regarding the occurrence of cystoid macular oedema, as this

	of Product Characteristics (SPC) and the corresponding changes to section 2 and 4 of the Package Leaflet (PL) have been carried out. Update of Summary of Product Characteristics and Package Leaflet				has been reported with Ganfort treatment. The resulting text in section 4.4 is the following "Cystoid macular oedema has been reported with GANFORT. Therefore, GANFORT should be used with caution in patients with known risk factors for macular oedema (e.g. aphakic patients, pseudophakic patients with a torn posterior lens capsule)." In section 4.8 of the SPC, "cystoid macular oedema" has been added as an adverse drug reaction. The package leaflet has been updated accordingly.
IA/0004	IA_15_a_Submission of Ph. Eur. certificate for active substance - approved manufacturer	31/10/2008	n/a		
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/02/2008	n/a	Labelling and PL	
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/08/2007	n/a	Labelling and PL	
IA/0001	IA_15_a_Submission of Ph. Eur. certificate for active substance - approved manufacturer	27/06/2007	n/a		