Azarga

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/0048/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure	11/10/2022		SmPC 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).

	concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation				
II/0045	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	28/10/2021	n/a		
IAIN/0047/G	This was an application for a group of variations. 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 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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	24/09/2021	19/05/2022	Annex II and PL	
IA/0046	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	24/08/2021	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
IB/0044	C.I.3.a - 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 - Implementation of wording agreed by the competent authority	22/07/2020	19/05/2022	SmPC and PL	
PSUSA/433/201904	Periodic Safety Update EU Single assessment - brinzolamide / timolol	28/11/2019	n/a		PRAC Recommendation - maintenance
IA/0042/G	This was an application for a group of variations. B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the	11/07/2019	n/a		

	dossier) - Replacement or addition of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
IA/0041	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	24/05/2019	n/a		
IA/0040	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/06/2018	20/06/2019	SmPC, Annex II, Labelling and PL	
T/0039	Transfer of Marketing Authorisation	20/03/2018	19/04/2018	SmPC, Labelling and PL	
IB/0038	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	26/02/2018	n/a		
T/0037	Transfer of Marketing Authorisation	06/04/2017	16/05/2017	SmPC, Labelling and PL	
II/0034	Update of sections 4.2, 4.4, 4.6 and 4.8 of the SmPC following a review of the safety profile taking into consideration data from clinical studies and post-marketing experience. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in	21/04/2017	19/04/2018	SmPC, Labelling and PL	The following new ADRs were added to SmPC section 4.8: white blood cell count (uncommon); anaphylactic shock (frequency not known); heart rate decreased (common); oropharyngeal pain (rare); rhinorrhoea (rare); blood urine present (uncommon). In addition, certain already labelled ADRs were allocated to a different frequency category.

	the SmPC, labelling and Package Leaflet and to update the contact details for the local representative in Spain in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				SmPC section 4.6 was updated to clarify that no studies have been performed to evaluate the effect of topical ocular administration of Azarga on human fertility. The changes to sections 4.2 and 4.4 of the SmPC were very minor and/or editorial. The Package Leaflet was updated to emphasise (in line with the SmPC) that the use of the product should be discontinued if signs of serious reactions or hypersensitivity occur, and to highlight that increase in pupil size when taking Azarga and adrenaline (epinephrine) together has been reported occasionally.
II/0035/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 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.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product 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	23/03/2017	n/a		

	size B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-				

	significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - 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 B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition 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				
IB/0036/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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - 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	23/02/2017	n/a		

	or addition) for the AS or a starting material/intermediate				
PSUSA/433/201604	Periodic Safety Update EU Single assessment - brinzolamide / timolol	01/12/2016	n/a		PRAC Recommendation - maintenance
IA/0033	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	03/08/2016	n/a		
IA/0031	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	13/08/2014	n/a		
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/0028	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information of Azarga eye drops, following a review of the available clinical data supporting the safety of the product. The Package Leaflet was updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/03/2014	19/03/2015	SmPC, Annex II and PL	Summary The MAH undertook a review of the available data supporting the safety profile of Azarga (10 mg/ml brinzolamide + 5 mg/ml timolol) 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 included ("After the cap is removed, if the tamper evident snap collar is loose, remove before using product")

					One new possible side effect (skin inflammation) was added to the Product Information.
IB/0029	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	27/11/2013	n/a		
IAIN/0027	B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	27/08/2013	n/a		
R/0023	Renewal of the marketing authorisation.	27/06/2013	26/08/2013	SmPC, Annex II, Labelling and PL	Based on the review of the cumulative efficacy and safety data available from clinical trials, post-marketing studies and spontaneous reports as well as the scientific literature, the CHMP concluded that there were no major changes to the known benefits and safety concerns associated with Azarga when used in the approved indication. The CHMP therefore concluded that the benefit/risk balance of Azarga to decrease intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension for whom monotherapy provides insufficient IOP reduction remained favourable and recommended the renewal of the marketing authorisation with unlimited validity.
IG/0324	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/07/2013	n/a		
II/0021	Update of sections 4.4, 4.5, 4.6, 4.7, 4.8 and 4.9 of the SmPC in order to update the safety information in line with the latest Company Core Safety	27/06/2013	26/08/2013	SmPC, Annex II, Labelling and PL	To reflect a review based on pooled data from seven clinical trials, post-marketing experience and a literature review carried out by the MAH, which, whilst not identifying new

	Information (CCSI) document. The Package Leaflet was 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				safety concerns, led to a general update of the safety information of Azarga. In summary, the text on possible occurrence of allergic reactions for both active ingredients of Azarga, was strengthened, since systemic absorption of these might occur. For the same reason, the text in relation to class effects for medicines called sulphonamides (one ingredient of Azarga is a sulphonamide) to inform on the risk of metabolic acidosis in patients at risk of renal impairment, and for beta-blockers (one other ingredient of Azarga is a beta blocker) to inform on the risk of muscle weakness was improved. The CHMP considered the proposals for the SmPC and the PL to be acceptable and overall improve the text of the prescribing and patient information.
IA/0025	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)	21/03/2013	n/a		
IG/0274	A.1 - Administrative change - Change in the name and/or address of the MAH	19/03/2013	26/08/2013	SmPC, Labelling and PL	
IA/0020	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 currently approved batch size	10/08/2012	n/a		

N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/04/2012	20/09/2013	PL	
IG/0149/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	06/03/2012	06/03/2012	Annex II	
IB/0015/G	This was an application for a group of variations. 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 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	17/02/2012	20/09/2013	SmPC and PL	1. The essential safety information detailed in the Pharmacovigilance Working Party (PhVWP) recommendations for Azarga which resulted from a class review of systemic effects of ophthalmic beta-blockers. 2. Recommendatins from CHMP following assessment of PSUR 005 that the adverse event depression is reflected under undesirable effects observed with Azarga at an unknow frequency. Additionally, the Danish PL has been corrected to include missing information.
IG/0145	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	09/02/2012	n/a		

IG/0107/G	This was an application for a group of variations. C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD	19/09/2011	n/a		
IG/0072	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	07/06/2011	n/a		
WS/0075	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To replace the current resin which is used for the closures for the drop-trainer packaging system, with two new resins. B.II.e.1.a.3 - Change in immediate packaging of the	20/01/2011	04/02/2011		

	finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products				
IB/0007	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 currently approved batch size	25/01/2011	n/a		
IA/0006/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	07/12/2010	n/a	Annex II	
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/12/2010	n/a	PL	
IG/0019	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur.	14/09/2010	n/a		

	Monograph - Updated certificate from an already approved manufacturer				
IB/0004	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	01/06/2010	n/a		
II/0003	To update the testing and specification of drug substance. Quality changes	21/01/2010	09/02/2010		
II/0002	To add an alternate manufacturing site for the manufacture of brinzolamide which is the active substance for Azarga. Quality changes	21/01/2010	09/02/2010		
II/0001	Addition of a new manufacturing site for the manufacture and batch release of the finished product Azarga and two contract sterilisation sites for the packaging materials. Quality changes	19/11/2009	21/12/2009	Annex II and PL	