Ulunar Breezhaler

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
IG/1801	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	29/11/2024		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).

IG/1788/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.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 A.7 - Administrative change - Deletion of manufacturing sites 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 where batch control/testing takes place	14/11/2024	n/a		
IG/1761/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	22/07/2024	n/a		

	procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
IG/1760	A.7 - Administrative change - Deletion of manufacturing sites	18/06/2024	n/a		
IB/0051/G	This was an application for a group of variations. 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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.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.III.1.a.2 - Submission of a new/updated or	17/06/2024	n/a		

	deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
PSUSA/10105 /202309	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	16/05/2024	n/a		PRAC Recommendation - maintenance
IG/1726	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	15/03/2024	n/a		
IG/1721/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	13/03/2024	n/a		
IG/1663	B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms	21/09/2023	n/a		
IG/1648/G	This was an application for a group of variations. 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 A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder	01/09/2023	n/a		

	or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient 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.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				
IB/0045/G	This was an application for a group of variations. 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.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.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	10/05/2023	n/a		

	batch control/testing takes place B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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.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.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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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.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) 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.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.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products				
IG/1513	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	17/05/2022	n/a		
IB/0043/G	This was an application for a group of variations. B.II.a.3.b.6 - Changes in the composition (excipients) of the finished product - Other excipients - Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	20/01/2022	n/a		

WS/2103	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	30/09/2021	n/a		
IG/1424/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.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	06/08/2021	15/11/2021	Annex II and PL	
IG/1406/G	This was an application for a group of variations. 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 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)	05/07/2021	n/a		

PSUSA/10105 /202009	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	10/06/2021	n/a		PRAC Recommendation - maintenance
IB/0039	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	08/01/2021	n/a		
IG/1306	B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier	21/12/2020	n/a		
IG/1305/G	This was an application for a group of variations. 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 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)	24/11/2020	n/a		
WS/1932	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	12/11/2020	15/11/2021	SmPC, Labelling and PL	
IG/1158/G	This was an application for a group of variations.	20/12/2019	n/a		

	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.7 - Administrative change - Deletion of manufacturing sites				
IG/1183	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	19/12/2019	09/03/2020	Annex II and PL	
WS/1543	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final study report of the Category I Post-Authorisation Safety Study (PASS) CQVA149A2402 (Multinational database cohort study in Europe in COPD patients, to assess the incidence rates and hazard ratios of various safety outcomes in new users of indacaterol/glycopyrronium compared to new users of comparator drugs (at the drug-class level). The Product Information has been updated by the removal of the black triangle and amendments in Annex II.D (Conditions or restrictions with regard to the safe and effective use of the medicinal product). The RMP version 5.0 has been submitted accordingly. C.I.11.b - Introduction of, or change(s) to, the	16/05/2019	09/03/2020	SmPC, Annex II and PL	Results of the study showed that a statistically significant increased incidence of all-cause mortality was identified for the QVA149 treatment cohort when compared to the Fixed-/Free LABA+LAMA. There was a tendency towards more patients treated with QVA149 as compared to the other Fixed/Free LABA+LAMA cohorts, developing a Major Cardiovascular Endpoint. There is no mechanistic or biologic reason to believe that QVA149 should increase mortality compared to other fixed or free combination (-product)s of LABA+LAMA therefore the observed imbalance does not represent a true safety finding. In addition, despite including real-world data and including a high number of patients in each treatment cohort, a number of limitations were observed with the study and generalisation of the results cannot be made. Overall, the study is confounded with multiple biases limiting any firm conclusions. Routine pharmacovigilance activities are considered sufficient. Changes in the product information relate only 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				deletion of the PASS commitment in Annex II and consequent removal from the list of additional monitoring (black triangle) in the SmPC and Package Leaflet.
WS/1570	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.z - Quality change - Finished product - Other variation	28/03/2019	09/03/2020	SmPC, Labelling and PL	
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/02/2019	09/03/2020	PL	
R/0028	Renewal of the marketing authorisation.	15/11/2018	15/01/2019	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Ulunar Breezhaler in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
WS/1448/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.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	13/09/2018	n/a		

	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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0027	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	26/07/2018	n/a		
IG/0957/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.7 - Administrative change - Deletion of manufacturing sites 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	28/06/2018	n/a		
T/0024	Transfer of Marketing Authorisation	26/03/2018	08/05/2018	SmPC, Labelling and PL	

PSUSA/10105 /201709	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	12/04/2018	n/a		PRAC Recommendation - maintenance
WS/1340	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	12/04/2018	n/a		
WS/1254/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. A.7 - Administrative change - Deletion of manufacturing sites 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.1.g - 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 not supported by an ASMF and requires significant update to the relevant AS section in the dossier	14/12/2017	n/a		
IB/0021/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name	06/12/2017	n/a		

	and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products 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				
IB/0019/G	This was an application for a group of variations. 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.IV.1.z - Change of a measuring or administration device - Other variation	24/10/2017	08/05/2018	SmPC, Labelling and PL	
WS/1247/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.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	28/09/2017	n/a		

	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
IG/0837	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	21/09/2017	n/a		
PSUSA/10105 /201609	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	06/04/2017	n/a		PRAC Recommendation - maintenance
WS/1005	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.8 of the Summary of Product Characteristics (SmPC) to add dysphonia and to bring up to date the list of adverse drug reactions and frequencies following a MAH's comprehensive review of all safety data. Section 4.4 of the SmPC was updated with regards the warning on paradoxical bronchospasm accordingly. The Package Leaflet (PL) is updated accordingly. The MAH also took this opportunity to update the Product Information as per the latest QRD template. A new Risk Management Plan (RMP) version (version 2.1) has been approved. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	10/11/2016	13/10/2017	SmPC, Labelling and PL	A comprehensive review of all safety data, performed by the MAH, following the conclusion of two recent clinical studies, CQVA149A2339 and CQVA149A2318 led to the update of all listed adverse drug reactions in section 4.8 of the SmPC. Hypersensitivity, Hyperglycaemia and diabetes mellitus and Bladder obstruction and urinary retention are now listed as common reported ADRs. Gastroenteritis and musculoskeletal pain are now listed under uncommonly reported ADRs and paraesthesia as a rare ADR. The warning regarding paradoxical bronchospasm is updated to reflect that this may happen during treatment as with other inhalation therapies. Dysphonia is identified as a new ADR uncommonly reported during the treatment and is added to section 4.8 of the SmPC. The PL is updated accordingly and Annex II, Annex IIIA have been brought in line with the latest QRD template.

	data				
WS/1004	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 5.1 of the summary of product characteristics (SmPC) to reflect the final results of study CQVA149A2318 "A 52-week treatment, multi-center, randomised, double-blind, double dummy, parallel-group, active controlled study to compare the effect of QVA149 (indacaterol maleate/glycopyrronium bromide) with salmeterol/fluticasone (salm/flut) on the rate of exacerbations in subjects with moderate to very severe COPD". In addition, the MAH took this opportunity to more accurately reflect the mean pre-dose values at week 64 from clinical study CQVA149A2304 report, included in the original marketing authorisation application. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/10/2016	13/10/2017	SmPC	The 52-week study compared QVA149 (indacaterol maleate/glycopyrronium bromide) (n=1,675) and fluticasone/salmeterol (n=1,679). QVA149 met the primary study objective of non-inferiority in rate of all COPD exacerbations (mild, moderate or severe) compared to fluticasone/salmeterol. The number of all COPD exacerbations/patient-years was 3.59 for QVA149 (4,531 events) and 4.03 for fluticasone/salmeterol (4,969 events). QVA149 further showed superiority in reducing the annualised rate of all exacerbations by 11% versus fluticasone/salmeterol (p=0.003). Results also showed a significant effect on health related quality of life measured using the St. George's Respiratory Questionnaire (SGRQ) as indicated by a reduction in SGRQ total score at 52 weeks compared to fluticasone/salmeterol (LS mean treatment difference 1.3, p=0.003).
IG/0712	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)	03/08/2016	n/a		

PSUSA/10105 /201509	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	14/04/2016	n/a		PRAC Recommendation - maintenance
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/01/2016	13/10/2017	PL	
IB/0009/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process 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	09/10/2015	22/01/2016	SmPC, Labelling and PL	
PSUSA/10105 /201503	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	08/10/2015	n/a		PRAC Recommendation - maintenance

IG/0568	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/05/2015	n/a		
PSUSA/10105 /201409	Periodic Safety Update EU Single assessment - indacaterol / glycopyrronium bromide	10/04/2015	n/a		PRAC Recommendation - maintenance
IG/0518	A.1 - Administrative change - Change in the name and/or address of the MAH	21/01/2015	22/01/2016	SmPC, Labelling and PL	
PSUV/0002	Periodic Safety Update	23/10/2014	16/12/2014	SmPC and PL	Please refer to Ulunar Breezhaler PSUV-02 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IG/0443	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)	20/08/2014	n/a		
IB/0003	B.II.e.7.z. - Change in supplier of packaging components or devices (when mentioned in the dossier) - Other variation	15/08/2014	n/a		
IB/0001	B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products	12/06/2014	n/a		