Ultibro 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
IB/0028	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	26/07/2018	n/a		
T/0025	Transfer of Marketing Authorisation	13/06/2018	23/07/2018	SmPC, Labelling and PL	
IG/0957/G	This was an application for a group of variations.	28/06/2018	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).

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	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				
R/0024	Renewal of the marketing authorisation.	22/03/2018	22/05/2018	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Ultibro Breezhaler in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
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.	14/12/2017	n/a		

	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				
IB/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.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	06/12/2017	n/a		

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	22/05/2018	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) 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	28/09/2017	n/a		
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.	10/11/2016	30/10/2017	SmPC, Labelling and	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

	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 data			PL	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.
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".	27/10/2016	30/10/2017	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

	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				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
IB/0010/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,	09/10/2015	28/01/2016	SmPC, Labelling and PL	

	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				
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	28/01/2016	SmPC, Labelling and PL	
PSUV/0003	Periodic Safety Update	23/10/2014	16/12/2014	SmPC and PL	Please refer to Ultibro Breezhaler PSUV-03 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/0004	B.II.e.7.z. - Change in supplier of packaging components or devices (when mentioned in the dossier) - Other variation	14/08/2014	n/a		

IB/0002	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	24/02/2014	n/a		
WS/0482	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Type IB worksharing to extend the shelf life of the finished product from based on real time data B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	23/01/2014	16/12/2014	SmPC	