



Tovanor 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
WS/2176	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p>	28/10/2021		SmPC, Annex II, Labelling 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/1459/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>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)</p>	27/10/2021	n/a		
WS/2103	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>	30/09/2021	n/a		
IG/1391	<p>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</p>	22/04/2021		SmPC, Annex II and PL	
IG/1376/G	<p>This was an application for a group of variations.</p> <p>A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release</p>	14/04/2021	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)				
IG/1347/G	<p>This was an application for a group of variations.</p> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> <p>B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits</p> <p>B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits</p> <p>B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p>	22/02/2021	n/a		
WS/1977	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation</p>	04/02/2021	n/a		
IG/1320/G	This was an application for a group of variations.	16/12/2020	n/a		

	<p>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</p> <p>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)</p>				
PSUSA/10047 /201909	Periodic Safety Update EU Single assessment - glycopyrronium bromide (for centrally authorised product indicated for chronic obstructive pulmonary disease)	14/05/2020	n/a		PRAC Recommendation - maintenance
IG/1197/G	<p>This was an application for a group of variations.</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>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</p>	28/01/2020	09/12/2020	Annex II and PL	
WS/1706	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and</p>	12/12/2019	09/12/2020	SmPC, Labelling and PL	

	Veterinary Medicinal Products - Other variation				
WS/1561	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	14/03/2019	n/a		
IG/1028/G	This was an application for a group of variations. 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	05/12/2018	n/a		
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/08/2018	09/12/2020	PL	
T/0030	Transfer of Marketing Authorisation	13/06/2018	09/07/2018	SmPC, Labelling and PL	
IB/0029/G	This was an application for a group of variations. 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	16/05/2018	n/a		

	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				
WS/1299	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Submission of the final study report of the Category 1 Post-Authorisation Safety Study (PASS) on cardio- and cerebrovascular outcomes (Multinational, multidatabase cohort study to assess adverse cardiovascular and cerebrovascular outcomes and mortality in association with inhaled NVA237 in Europe / CNVA237A2402T) with subsequent update of Annex II. Consequently, the deletion from the list of additional monitoring led to the update of Annex I and III B. The MAH also took this opportunity to update the local representatives. The RMP version 8 was submitted.</p> <p>C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation</p>	12/04/2018	09/07/2018	SmPC, Annex II and PL	Changes in the SmPC, PL and Annex II relate only to the deletion of the PASS commitment and consequent removal from the list of additional monitoring.
WS/1298	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.13 - Other variations not specifically covered</p>	12/04/2018	n/a		

	elsewhere in this Annex which involve the submission of studies to the competent authority				
WS/1247/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)</p> <p>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</p>	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		
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/08/2017	09/07/2018	PL	
R/0022	Renewal of the marketing authorisation.	18/05/2017	26/07/2017	SmPC, Labelling and PL	
IG/0816	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)	19/06/2017	n/a		

PSUSA/10047 /201609	Periodic Safety Update EU Single assessment - glycopyrronium bromide (for centrally authorised product indicated for chronic obstructive pulmonary disease)	06/04/2017	n/a		PRAC Recommendation - maintenance
IG/0750	B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier	02/12/2016	n/a		
WS/1002	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 DUS (CNVA237A2401T) and RMP update (version 6.0). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/09/2016	n/a		
WS/1001	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Revision of section 4.8 of SmPC to include a new ADR, Dysphonia. The PL is updated accordingly. The MAHs took the opportunity to update to the latest QRD template v10. The MAH also took the opportunity to update in Annex II the wording of the PASS study milestones,	15/09/2016	26/07/2017	SmPC, Annex II, Labelling and PL	Update to the product information to include the ADR Dysphonia with the frequency 'uncommon'. The wording of the latest QRD wording (version 10) was implemented.

	<p>following the assessment of ANX01 commitment to date.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>				
PSUSA/10047 /201509	Periodic Safety Update EU Single assessment - glycopyrronium bromide (for centrally authorised product indicated for chronic obstructive pulmonary disease)	14/04/2016	n/a		PRAC Recommendation - maintenance
IG/0630/G	<p>This was an application for a group of variations.</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p>	05/11/2015	n/a		
WS/0782	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.5 of the SmPC in order to add class labelling text regarding the concomitant use with some commonly used medicines. The Package Leaflet is updated accordingly.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	30/07/2015	12/05/2016	SmPC and PL	Although no formal drug interaction studies have been performed, Seebri Breezhaler has been used concomitantly with other medicinal products commonly used in the treatment of COPD without clinical evidence of drug interactions. These include sympathomimetic bronchodilators, methylxanthines, and oral and inhaled steroids.

WS/0781	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.8 of the SmPC in order to add pruritus with frequency uncommon and paradoxical bronchospasm with frequency not known as new ADRs based on post marketing reports already submitted in the PSUR 4 (EMA/H/C/PSUSA/00010047/201409). The Package Leaflet is updated accordingly. The MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	30/07/2015	12/05/2016	SmPC and PL	
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		
IB/0012/G	<p>This was an application for a group of variations.</p> <p>B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p>	19/05/2015	12/05/2016	SmPC, Labelling and PL	

	<p>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</p> <p>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process</p> <p>B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation</p> <p>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</p> <p>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</p> <p>A.1 - Administrative change - Change in the name and/or address of the MAH</p>				
PSUSA/10047 /201409	Periodic Safety Update EU Single assessment - glycopyrronium bromide (for centrally authorised product indicated for chronic obstructive pulmonary disease)	10/04/2015	n/a		PRAC Recommendation - maintenance
PSUV/0007	Periodic Safety Update	09/10/2014	n/a		PRAC Recommendation - maintenance
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		

N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2014	12/05/2016	PL	
PSUV/0004	Periodic Safety Update	25/04/2014	19/06/2014	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s) for PSUV/0004.
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/02/2014		PL	
IB/0005	B.II.e.7.z. - Change in supplier of packaging components or devices (when mentioned in the dossier) - Other variation	30/01/2014	n/a		
WS/0456	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.8 of the SmPC to accurately reflect the percentage of cases of dry mouth and section 5.1 to revise the p-values of trough FEV1 and the information on the reduction of COPD exacerbations in the pivotal studies A2304 and A2303. Furthermore, the MAH took this opportunity to bring the PI in line with the latest QRD template, to make minor editorial changes and to include the black triangle to reflect that the product is under additional monitoring.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p>	18/12/2013	19/06/2014	SmPC, Annex II and PL	<p>The clinical phase III development program for glycopyrronium bromide included two pivotal studies: a 6-month placebo-controlled study (CNVA237A2304) and a 12-month placebo and active-controlled (open label tiotropium 18 micrograms once daily) study (CNVA237A2303), both in patients with clinical diagnosis of moderate to severe COPD. The SmPC reflects the primary endpoint trough FEV1 for glycopyrronium bromide compared to placebo at the 6-month time-point (108mL) for study A2304 and at the 12-month time-point (97mL) for study A2303. In order to more precisely reflect the study results, the p-values for both studies are being changed from $p < 0.05$ to $p < 0.001$ in section 5.1 of the SmPC. In addition, the information related to the reduction of COPD exacerbations is being revised in section 5.1 of the SmPC to improve clarity and accuracy.</p> <p>The percentage of cases of "dry mouth" reported for</p>

					glycopyrronium bromide compared to placebo is 2.4% versus 1.1% for the MedDRA Preferred Term "dry throat". This was changed in order to reflect the actual number of patients with the MedDRA Preferred Term (PT) "dry mouth" in the 6-month database i.e. 2.2% versus 1.1% in accordance with the EPAR.
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/07/2013	19/06/2014	PL	Inclusion of an additional local representative of the MAH for the new Member State, Croatia.
IG/0248	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/12/2012	n/a		