Rolufta Ellipta

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
PSUSA/10263 /202112	Periodic Safety Update EU Single assessment - umeclidinium	15/09/2022	09/11/2022	SmPC and PL	Please refer to EPAR: scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
R/0019	Renewal of the marketing authorisation.	11/11/2021	07/01/2022	SmPC, Annex II, Labelling	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Rolufta

[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).

				and PL	Ellipta in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IG/1340	A.7 - Administrative change - Deletion of manufacturing sites	16/02/2021	07/01/2022	Annex II and PL	
IG/1330	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	22/01/2021	n/a		
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/12/2020	07/01/2022	PL	
WS/1589	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of an updated RMP version 7.2 following completion of a category 3 study (WWE117397) "A Post-authorization safety Electronic Medical Records database retrospective cohort study of new users of inhaled UMEC/VI or new users of inhaled UMEC in the primary care setting". In addition, updates are included relating to the Category 1 study 201038 "Post-authorisation Safety (PAS) Observational Cohort Study to Quantify the Incidence and Comparative Safety of Selected Cardiovascular and Cerebrovascular Events in COPD Patients Using Inhaled UMEC/VI Combination, or Inhaled UMEC	29/10/2020	n/a		The MAH submitted with this variation an updated RMP version 7.2. following completion of a category 3 study (WWE117397) to reflect the utilization among new users (including possible off-label prescribing) of these medications in a real-world, post-approval setting. In addition, updates are also included relating to the Category 1 study 201038 and agreed in procedure PSA/S/0032.3 which assessed substantial amendments to a non-interventional imposed PASS protocol in accordance with Article 107o of Directive 2001/83/EC. Those changes covered: Study title amended to align with the primary study objective, the primary and secondary objectives updated to include the composite endpoint and the sample size for the study. The reclassification of the safety concerns proposed by the MAH is acceptable.

	versus Tiotropium (Study201038).” The RMP is also updated to align with the Guidance on the Good Pharmacovigilance Practice (GVP) Module V - Risk management systems Revision 2 guidelines. 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				
WS/1863/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.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes 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	24/09/2020	n/a		

	control/testing takes place B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation				
WS/1761	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 report from study WWE117397 listed as a category 3 study in the RMP. This was a retrospective longitudinal non-interventional observational study of new users of inhaled umeclidinium/vilanterol (UMEC/VI) or new users of inhaled umeclidinium (UMEC) or new users or long-acting bronchodilators (LABD) in the primary care setting. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	09/07/2020	n/a		The primary objective of the study was to report the proportion of patients with a possible off-label use and characterize them in new users of UMEC/VI, UMEC, or other LABD. The second objective was to quantify incidence of major cardiovascular and cerebrovascular events, mortality and pneumonia, and rates of exacerbations of COPD during follow-up in new users of UMEC/VI or UMEC. The tertiary objective was in new users of UMEC/VI or UMEC with 12 or more months of follow-up following initiation, to describe treatment patterns and adherence. Despite the fact that several limitations were identified in data sources and did not allow to drawn sound conclusions for all the study objectives, the final report provides insight on UMEC and UMEC/VI utilisation patterns, including off-label prescribing rate of UMEC and UMEC/VI compared to other LABD in a primary care UK setting. Overall, the incidence of cardiovascular events and respiratory outcomes was as expected for these products classes, and no new safety signals were identified. Mortality rates reported in this study (using linked CPRD-HES-ONS) data are comparable to those reported using the same dataset for other LAMAs. The analysis of treatment patterns during the first 12 months after initiating treatment with UMEC or UMEC/VI showed a good level of continuity for the majority of new users. No major difference in treatment patterns of on-label or potential off-label use for both UMEC and UMEC/VI users was noted in all groups. It can also be concluded that in this setting the analysis reveals a

					moderate level of adherence to UMEC and UMEC/VI treatment. Overall, based on the data reviwed no change to the product information was deemed necessary.
IG/1159	A.1 - Administrative change - Change in the name and/or address of the MAH	29/11/2019	30/09/2020	SmPC, Annex II, Labelling and PL	
PSUSA/10263 /201812	Periodic Safety Update EU Single assessment - umeclidinium	25/07/2019	26/09/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10263/201812.
WS/1505	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 SmPC to add efficacy information based on the 52-week study CTT116855; a 52-week study designed to evaluate the efficacy of FF/UMEC/VI 100/62.5/25 compared with dual therapy of FF/VI 100/25 or UMEC/VI 62.5/25 in subjects with COPD. In addition, clarification on information related to the 24 week study submitted at time of initial authorisation is introduced in section 5.1. Update of section 4.8 of the SmPC to update the frequency of constipation from 'uncommon' to 'common'. The Package Leaflet is updated in accordance. The worksharing procedure leads to amendments to the Summary of Product Characteristics and Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) -	19/09/2019	30/09/2020	SmPC and PL	The procedure started as a modification of indication in order to reflect prevention on COPD exacerbations in the approved indication. The evaluation of the presented data led to an update of section 5.1 to describe information that may be relevant for the prescribers to take decisions in the step wise approach to COPD management. Results from the IMPACT study do not allow ascertaining the exact contribution of Incruse/Rolufta Ellipta to the reduction in the rate of exacerbations. However the data are considered relevant from the clinical point of view taking into account the known correlation between exacerbations and morbidity/mortality. The following data added to section 5.1: In the randomised, double-blind, 52-week study (CTT116855, IMPACT) of 10,355 adult patients with symptomatic COPD and a history of 1 or more moderate or severe exacerbations within the prior 12 months, treatment with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI 99/55/22 micrograms) once daily as a single inhaler was compared with fluticasone furoate/vilanterol (FF/VI 99/22 micrograms) once daily as a single inhaler. The primary endpoint was annual rate of on-treatment moderate

	Addition of a new therapeutic indication or modification of an approved one				and severe exacerbations in subjects treated with FF/UMC/VI compared with FF/VI. The mean annual rate of exacerbations was 0.91 and 1.07 for FF/UMEC/VI and FF/VI respectively (Rate Ratio: 0.85; 95% CI: 0.80, 0.90; p<0.001). At Week 52, a statistically significant improvement in the least-squares (LS) mean change from baseline in trough FEV1 was observed for FF/UMEC/VI compared with FF/VI (mean change: +94 mL vs. -3 mL; treatment difference: 97 mL; 95% CI: 85, 109; p<0.001). In addition, clarification on information related to the 24 week study submitted at time of initial authorisation is introduced in section 5.1 , in particular information on the severity of disease in the trial population studied in the 24 week efficacy study, as well as information on the risk ratios and confidence intervals. Furthermore, based on the frequency reported in the IMPACT study, the frequency of constipation has been amended from 'uncommon' to 'common' in section 4.8 of the SmPC. The Package leaflet is amended accordingly.
N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/04/2019	25/07/2019	Labelling and PL	
IG/1016	B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	16/01/2019	25/07/2019	Annex II and PL	
WS/1437/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.4 - Administrative change - Change in the name	20/09/2018	n/a		

	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 B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition				
PSUSA/10263 /201712	Periodic Safety Update EU Single assessment - umeclidinium	06/09/2018	n/a		PRAC Recommendation - maintenance
IG/0959	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	10/08/2018	25/07/2019	SmPC, Annex II, Labelling and PL	
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/06/2018	25/07/2019	PL	
WS/1276/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.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing	22/03/2018	n/a		

	processes				
IB/0002/G	This was an application for a group of variations. C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	18/07/2017	21/06/2018	SmPC and PL	
WS/1191	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/07/2017	21/06/2018	SmPC and PL	