Colobreathe

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/0063	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	18/12/2024		Labelling	To remove the additional risk minimization measures from Annex II in order to align with the currently approved RMP.
IB/0062	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	27/09/2024	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).

	authorisation, including the RMP - Other variation				
T/0061	Transfer of Marketing Authorisation	09/04/2024	25/04/2024	SmPC, Labelling and PL	
IB/0060	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	12/02/2024	n/a		
IAIN/0059/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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	09/11/2023	n/a		
N/0058	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/10/2023	25/04/2024	Labelling and PL	
PSUSA/9112/ 202302	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	28/09/2023	n/a		PRAC Recommendation - maintenance
IB/0057/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any	10/08/2023	25/04/2024	Annex II and PL	

	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 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.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.z - Quality change - Finished product - Other variation B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IA/0055	A.7 - Administrative change - Deletion of manufacturing sites	10/05/2023	25/04/2024	Annex II and PL	
IB/0054	B.II.f.z - Stability of FP - Other variation	17/02/2023	n/a		

IA/0053	B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms	04/01/2023	n/a		
IG/1561	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)	18/11/2022	n/a		
IA/0051/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	03/11/2022	n/a		

IB/0050/G	This was an application for a group of variations. B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	20/04/2022	n/a		
N/0049	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/01/2022	25/04/2024	PL	
IB/0048	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	05/10/2020	29/09/2021	SmPC, Annex II, Labelling and PL	
PSUSA/9112/ 202002	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	03/09/2020	n/a		PRAC Recommendation - maintenance
IAIN/0046/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	04/03/2020	10/08/2020	Annex II and PL	

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place 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				
II/0044/G	This was an application for a group of variations. 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 C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	13/02/2020	n/a		
IA/0045/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 procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	04/10/2019	n/a		
PSUSA/9112/ 201902	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	05/09/2019	n/a		PRAC Recommendation - maintenance

IAIN/0043	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	28/08/2019	10/08/2020	Annex II and PL	
II/0039	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/02/2019	n/a		
IA/0041/G	This was an application for a group of variations. 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.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	19/12/2018	n/a		
IA/0040	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	05/12/2018	n/a		
PSUSA/9112/ 201802	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	06/09/2018	n/a		PRAC Recommendation - maintenance

IAIN/0038/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.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.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	08/08/2018	19/07/2019	Annex II and PL	
IB/0036	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	17/11/2017	n/a		
PSUSA/9112/ 201702	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	01/09/2017	n/a		PRAC Recommendation - maintenance
IAIN/0035	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	17/08/2017	n/a		
IAIN/0034/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites	17/08/2017	n/a		

	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
II/0031	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	22/06/2017	n/a		
IAIN/0033	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	01/06/2017	n/a		
II/0023	Change to the composition of the capsules from hard gelatin to hard PEG-gelatin capsules, which are standard gelatin capsules containing polyethylene glycol as an additional plasticizer (5% w/w PEG). The requested variation proposed amendments to the Summary of Product Characteristics. B.II.a.3.b.2 - Changes in the composition (excipients) of the finished product - Other excipients - Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the product	23/02/2017	30/01/2018	SmPC and PL	
IB/0029	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	16/02/2017	n/a		
T/0028	Transfer of marketing authorisation from Forest Laboratories UK Limited to Teva B.V., Netherlands.	28/11/2016	12/12/2016	SmPC, Labelling and	

	Transfer of Marketing Authorisation			PL	
R/0024	Renewal of the marketing authorisation.	21/07/2016	26/09/2016	SmPC, Annex II, Labelling and PL	
IA/0027/G	This was an application for a group of variations. 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.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	07/09/2016	n/a		
PSUSA/9112/ 201602	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	02/09/2016	n/a		PRAC Recommendation - maintenance
II/0021	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	23/06/2016	n/a		
IAIN/0025	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	03/05/2016	n/a		
IA/0022	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test	21/12/2015	n/a		

	procedure				
PSUSA/9112/201502	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	10/09/2015	n/a		PRAC Recommendation - maintenance
IAIN/0020	A.1 - Administrative change - Change in the name and/or address of the MAH	12/06/2015	19/11/2015	SmPC, Labelling and PL	
IAIN/0018	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	11/05/2015	n/a		
A31/0007	On 16 September 2013, the European Commission initiated a referral under Article 31 of Directive 2001/83/EC. The CHMP was requested to give its opinion on the benefit-risk of polymyxin-based products and on the need for regulatory measures to be taken. A review under Article 5(3) of Regulation (EC) No 726/2004 of manufacturing and quality control methods was also conducted.	23/10/2014	11/03/2015		For further information please refer to the Polymyxin-based products Art 31 referral (EMEA/H/A-31/1383) CHMP assessment report.
PSUSA/9112/201408	Periodic Safety Update EU Single assessment - colistimethate sodium (dry inhalation powder)	12/02/2015	n/a		PRAC Recommendation - maintenance
IA/0017	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	28/11/2014	19/11/2015	SmPC	

II/0015	Update of sections 4.2 and 6.6 of the SmPC in order to update the information on the administration of the product following Focus Testing on the Package Leaflet. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/09/2014	16/12/2014	SmPC and PL	Following the conduct of Focus Test and an Addendum to the Focus Test on the Package Leaflet for Colobreathe, the MAH updated sections 4.2 and 6.6 of the SmPC in order to update the information on the administration of the product. The Package Leaflet is updated accordingly. The changes were reviewed and deemed acceptable to the CHMP.
PSUV/0014	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
PSUV/0009	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
II/0010	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	20/02/2014	n/a		
IAIN/0012/G	This was an application for a group of variations. B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale B.II.f.1.e - Stability of FP - Change to an approved stability protocol	08/01/2014	31/07/2014	SmPC	
IA/0011	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	08/01/2014	n/a		

II/0005	Update of sections 4.4, 4.5 and 5.2 of the SPC with results from absorption study COLO-DPI-02-11 carried out to confirm pharmacokinetics of colistimethate sodium via inhalation powder. The Package Leaflet is updated accordingly. Updates to the "Non-clinical Overview" and "Clinical Overview" have also been submitted. The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/11/2013	31/07/2014	SmPC and PL	A 7-Day Open-Label Pharmacokinetic Study (COLO-DPI-02-11) to investigate the Systemic Absorption of Colistimethate Sodium after Inhalation of Dry Powder Colistimethate Sodium for Inhalation (Colobreathe 125mg) was conducted in Adult, Adolescent and Paediatric Cystic Fibrosis Subjects with Chronic Pulmonary Infection with Pseudomonas aeruginosa. The primary objective was to assess the magnitude of systemic exposure to colistimethate and its active breakdown products after repeat dosing with Colobreathe in adult, adolescent, and paediatric subjects with cystic fibrosis (CF). The results of this study showed minimal absorption of colistin and colistimethate after inhalation of Colobreathe. A validated LC-MS/S method was used to measure the concentration of colistin and colistimethate was calculated indirectly through colistin measurements. The obtained values were lower that what has been obtained after administration of I.V injections / nebulised administration of colistimethate sodium (CMS). A high concentration of total CMS and total free colistin were observed in sputum for all subjects and a minimal amount of colistin was found in urine. Appropriate statements are introduced in the Product Information, also expressing caution with concomitant use of other colistimethate formulations agents since data are missing on possible additive effects. Caution has to be applied with use of Colobreathe with parenteral or nebulised treatment with colistimethate sodium and with nephrotoxic or neurotoxic agents. The benefit/risk balance of Colobreathe is considered to

					remain positive.
IAIN/0008	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	04/11/2013	n/a		
IAIN/0006	B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	05/08/2013	31/07/2014	Annex II and PL	
IB/0003/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.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	02/08/2013	31/07/2014	SmPC, Labelling and PL	
IAIN/0004	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	27/05/2013	n/a		
IAIN/0002/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.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	19/07/2012	n/a		

	C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database 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 C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities 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				
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/06/2012	31/07/2014	Labelling and PL	