



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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 |
|--------------------|--|--|--|---|---------|
| 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 | | |

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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| IAIN/0059/G | <p>This was an application for a group of variations.</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> <p>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</p> | 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 | <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.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</p> <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> | 10/08/2023 | 25/04/2024 | Annex II and PL | |

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| | <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.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> <p>B.II.z - Quality change - Finished product - Other variation</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> <p>B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> | | | | |
| 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 | 18/11/2022 | n/a | | |

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| | (excluding manufacturer for batch release) | | | | |
| IA/0051/G | <p>This was an application for a group of variations.</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> | 03/11/2022 | n/a | | |
| IB/0050/G | <p>This was an application for a group of variations.</p> <p>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</p> | 20/04/2022 | n/a | | |

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| | <p>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</p> <p>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</p> | | | | |
| 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 | <p>This was an application for a group of variations.</p> <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.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.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer</p> | 04/03/2020 | 10/08/2020 | Annex II and PL | |

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| | 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 - | 28/08/2019 | 10/08/2020 | Annex II and PL | |

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| | Not including batch control/testing | | | | |
| 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 | 08/08/2018 | 19/07/2019 | Annex II and PL | |

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| | <p>arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place</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> <p>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</p> | | | | |
| 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 | <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.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> | 17/08/2017 | n/a | | |

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| 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. Transfer of Marketing Authorisation | 28/11/2016 | 12/12/2016 | SmPC, Labelling and PL | |

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| 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 procedure | 21/12/2015 | n/a | | |

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| PSUSA/91112/201502 | 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 (EMA/H/A-31/1383) CHMP assessment report. |
| PSUSA/91112/201408 | 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 | 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 |

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| | <p>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.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p> | | | | 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 | <p>This was an application for a group of variations.</p> <p>B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale</p> <p>B.II.f.1.e - Stability of FP - Change to an approved stability protocol</p> | 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 | | |

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| II/0005 | <p>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.</p> <p>The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet.</p> <p>C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data</p> | 21/11/2013 | 31/07/2014 | SmPC and PL | <p>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.</p> <p>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).</p> <p>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.</p> <p>The obtained values were lower than what has been obtained after administration of I.V injections / nebulised administration of colistimethate sodium (CMS).</p> <p>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.</p> <p>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.</p> <p>The benefit/risk balance of Colobreathe is considered to</p> |
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| | | | | | 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 | | |

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| | <p>C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database</p> <p>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</p> <p>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</p> <p>C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities</p> <p>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</p> | | | | |
| 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 | |