



Edistride

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 |
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| WS/2733 | 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 | 05/09/2024 | 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).



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| | of studies to the competent authority | | | | |
| PSUSA/10029/202310 | Periodic Safety Update EU Single assessment - dapagliflozin | 30/05/2024 | 01/08/2024 | SmPC | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10029/202310. |
| WS/2652/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.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> | 27/06/2024 | n/a | | |
| WS/2662/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.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.e - Replacement or addition of a</p> | 25/04/2024 | n/a | | |

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| | 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 | | | | |
| IG/1693 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 06/02/2024 | 28/06/2024 | SmPC and PL | |
| WS/2362 | <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.1.d - Replacement or addition of a manufacturing site for the FP - Site which requires an initial or product specific inspection</p> <p>B.II.b.1.d - Replacement or addition of a manufacturing site for the FP - Site which requires an initial or product specific inspection</p> | 14/12/2023 | n/a | | |
| WS/2517 | <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 an updated RMP version 30 in order to remove the potential important risk for Lower Limb Amputation.</p> <p>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</p> | 28/09/2023 | n/a | | |

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| | by new additional data to be submitted by the MAH where significant assessment is required | | | | |
| IG/1630 | 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) | 26/06/2023 | n/a | | |
| IG/1616 | A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release | 30/05/2023 | 28/06/2024 | Annex II and PL | |
| WS/2439/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.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> | 12/05/2023 | n/a | | |

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| <p>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> <p>B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> | | | | |
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| <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> <p>B.I.b.2.c - Change in test procedure for AS or</p> | | | | |
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| | <p>starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> | | | | |
| PSUSA/10029 /202210 | Periodic Safety Update EU Single assessment - dapagliflozin | 12/05/2023 | n/a | | PRAC Recommendation - maintenance |
| WS/2421 | <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>Please refer to the Recommendations section</p> <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p> | 14/04/2023 | n/a | | Not applicable |
| WS/2299 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. | 15/12/2022 | 23/01/2023 | SmPC and PL | |

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| | <p>Please refer to the Recommendations section.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p> | | | | |
| PSUSA/10029 /202110 | <p>Periodic Safety Update EU Single assessment - dapagliflozin</p> | 19/05/2022 | 15/07/2022 | SmPC and PL | <p>Please refer to EDISTRIDE, FORXIGA PSUSA-10029-202110 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation</p> |
| WS/2284 | <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> | 23/06/2022 | n/a | | <p>The PDCO has confirmed compliance with the agreed completed paediatric investigation plan as adopted November 2021. Therefore the statement indicating compliance with the agreed completed PIP has been confirmed.</p> |
| WS/2234/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>A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> | 02/06/2022 | n/a | | |

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| IG/1498/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.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> | 01/04/2022 | 15/07/2022 | Annex II and PL | |
| WS/1952 | <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>Extension of indication for Forxiga / Edistride to include treatment of children aged 10 years and adolescents with T2DM based on the results from studies MB10209/D1690C000016 and MB102-138/D1690C00017; these are paediatric studies submitted according to Article 46 of the Paediatric Regulation. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 21 of the RMP has also been submitted.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p> | 14/10/2021 | 12/11/2021 | SmPC and PL | Please refer to Scientific Discussion dapagliflozin (Forxiga/ Edistride) 'Procedure No. EMEA/H/C/WS1952. |
| PSUSA/10029 /202104 | Periodic Safety Update EU Single assessment - dapagliflozin | 28/10/2021 | n/a | | PRAC Recommendation - maintenance |

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| WS/1941 | <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>Extension of Indication to add the treatment of chronic kidney disease in adults. Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated for Forxiga and Edistride based on the results from the renal outcomes study D169AC00001 (DAPA-CKD), and the Annex II.B and Package Leaflet of these products are updated accordingly. The DAPA-CKD study is a category 3, Post-Authorisation Safety Study (PASS) listed in the dapagliflozin RMP to evaluate the potential risk of lower limb amputation; it is a multicentre, event-driven, randomized, double-blind, parallel group, placebo-controlled study, evaluating the effect of dapagliflozin versus placebo, given once daily in addition to standard of care, to prevent the progression of chronic kidney disease (CKD) or cardiovascular (CV)/renal death.</p> <p>In addition, the Risk Management Plan for dapagliflozin (version 25s3) has been updated.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p> | 24/06/2021 | 23/07/2021 | SmPC, Annex II and PL | Please refer to Scientific Discussion Forxiga/ Edistride - EMEA/H/C/WS1941 |
| WS/2069/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> | 10/06/2021 | n/a | | |

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| | <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p> <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p> | | | | |
| IG/1401/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.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site</p> | 04/06/2021 | n/a | | |
| PSUSA/10029 /202010 | <p>Periodic Safety Update EU Single assessment - dapagliflozin</p> | 06/05/2021 | n/a | | PRAC Recommendation - maintenance |
| WS/2009/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>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p> <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p> <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p> | 09/04/2021 | n/a | | |

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| | elsewhere in this Annex which involve the submission of studies to the competent authority | | | | |
| IG/1367 | B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size | 15/03/2021 | n/a | | |
| IG/1335/G | This was an application for a group of variations. 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 A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites | 12/02/2021 | 23/07/2021 | Annex II and PL | |
| WS/1737 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC for Edistride and Forxiga to add a new indication for the treatment of symptomatic heart failure with reduced ejection fraction in adults. The Package Leaflet and Labelling are updated in accordance. The RMP version 19.6 is agreed as part of this procedure. | 15/10/2020 | 03/11/2020 | SmPC, Labelling and PL | Please refer to Scientific Discussion 'Forxiga-H-C-002322-WS1737' and/or 'Edistride-H-C-04161/WS1737' |

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| | <p>Furthermore, the PI is brought in line with the latest QRD template version 10.1, as well as editorial change (addition of SI unit for blood glucose).</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p> | | | | |
| PSUSA/10029 /202004 | Periodic Safety Update EU Single assessment - dapagliflozin | 29/10/2020 | n/a | | PRAC Recommendation - maintenance |
| R/0038 | Renewal of the marketing authorisation. | 23/07/2020 | 25/09/2020 | SmPC, Annex II, Labelling and PL | <p>Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Edistride in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.</p> <p>During the procedure, the MAH withdrew the indication for type 1 diabetes mellitus (business decision). The SmPC and package leaflets for the 5 mg and 10mg strength have been combined, and its content and Annex II have been updated accordingly.</p> |
| WS/1853/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.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor</p> | 03/09/2020 | n/a | | |

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| | <p>changes to an approved test procedure</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> <p>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS</p> | | | | |
| WS/1742 | <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.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> | 14/05/2020 | n/a | | |

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| PSUSA/10029 /201910 | Periodic Safety Update EU Single assessment - dapagliflozin | 17/04/2020 | n/a | | PRAC Recommendation - maintenance |
| IG/1171 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 11/12/2019 | 25/09/2020 | SmPC and PL | |
| WS/1692/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.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.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.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> | 14/11/2019 | n/a | | |
| WS/1637 | <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 sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) of</p> | 17/10/2019 | 25/09/2020 | SmPC and PL | Information on Fournier`s gangrene in section 4.8 was updated with the frequency `very rare`, based on the DECLARE study and information was added under `Description of selected adverse reactions` ; a reference to section 4.8 was added in SmPC section 4.4. |

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| | <p>the SmPC of dapagliflozin-containing products with respect to the Fournier's gangrene class labelling language, following results from the DECLARE study (a Multicentre, Randomized, Double-Blind, Placebo-Controlled cardiovascular outcome trial in Patients with Type 2 Diabetes). 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> | | | | The Package Leaflet was updated accordingly. |
| WS/1539 | <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 sections 4.1 , 4.2, 4.4, 4.8, and 5.1 of the SmPC of Forxiga, Edistride, Xigduo and Ebymect to modify the indication and to reflect new data based on final results from study D1693C00001 (DECLARE). This was a multi-centre, randomised, double-blind, placebo-controlled study to evaluate the effect of dapagliflozin on cardiovascular (CV) and renal outcomes in patients with T2DM with or without established CV disease. The Package Leaflets (PL) are updated accordingly. The dapagliflozin Risk Management Plan (RMP) and dapagliflozin/metformin RMP have also been updated to version 17 and version 11 respectively.</p> <p>The Worksharing applicant took the opportunity to make editorial changes and bring the PI in line with</p> | 27/06/2019 | 25/07/2019 | SmPC and PL | Please refer to the Scientific Discussion 'EMA/H/C/xxxx/WS/1539' |

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| | <p>the updated excipient guideline (lactose wording in SmPC section 4.4) .</p> <p>The worksharing procedure leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p> | | | | |
| PSUSA/10029 /201810 | Periodic Safety Update EU Single assessment - dapagliflozin | 29/05/2019 | 19/07/2019 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s) for PSUSA/10029/201810. |
| WS/1344 | <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.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p> | 31/01/2019 | 20/03/2019 | SmPC, Annex II, Labelling and PL | |
| IG/1067 | 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 | 19/03/2019 | n/a | | |
| IG/1064 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 01/03/2019 | 19/07/2019 | SmPC and PL | |

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| WS/1380 | <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 sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the final study results from study D1690C00024 (DERIVE); A Multicentre, Double-Blind, Placebo-Controlled, Parallel Group, Randomized, Phase III Study to Evaluate the Glycaemic Efficacy and Renal Safety of Dapagliflozin in Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment (CKD 3A) Who Have Inadequate Glycaemic Control.</p> <p>In addition, the Worksharing applicant took the opportunity to implement minor editorial changes in Edistride, Ebymect and Xigduo PI and to update the list of local representatives in the Package Leaflets for Edistride and Ebymect.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> | 20/09/2018 | 12/11/2018 | SmPC and PL | <p>Based on the results from study D1690C00024 (DERIVE) the following dosage recommendation in case of renal impairment has been updated in section 4.2 and 4.4.</p> <p>Forxiga, Edistride: dapagliflozin should not be initiated in patients with a glomerular filtration rate [GFR] < 60 mL/min and should be discontinued at GFR persistently below 45 mL/min. No dosage adjustment is required based on renal function.</p> <p>Xigduo, Ebymect: the maximum daily dose of metformin should preferably be divided into 2-3 daily doses. Factors that may increase the risk of lactic acidosis should be reviewed before considering initiation of metformin in patients with GFR < 60 mL/min.</p> <p>The results of study D1690C00024 (DERIVE) have been reflected in section 5.1 of Edistride, Ebymect, Forxiga and Xigduo</p> |
| WS/1345/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.I.d.z - Stability of AS - Other variation B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol</p> | 19/04/2018 | n/a | | |

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| PSUSA/10029 /201710 | Periodic Safety Update EU Single assessment - dapagliflozin | 12/04/2018 | n/a | | PRAC Recommendation - maintenance |
| IG/0892 | 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 | 28/02/2018 | n/a | | |
| IG/0894 | 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 | 05/02/2018 | n/a | | |
| WS/1229 | 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 | 30/11/2017 | n/a | | |
| WS/1259 | 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 | 30/11/2017 | n/a | | |

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| IB/0021 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 06/11/2017 | 29/06/2018 | SmPC, Labelling and PL | |
| IG/0841 | B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | 24/10/2017 | n/a | | |
| WS/1167 | <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 sections 4.8 and 5.1 of the SmPC in order to add information regarding two initial combination studies (MB102021 and MB102034) in treatment-naïve patients of dapagliflozin 5 mg + metformin and dapagliflozin 10 mg + metformin, respectively, compared to each component separately.</p> <p>In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> | 12/10/2017 | 29/06/2018 | SmPC and Labelling | |
| WS/1198 | <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.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing</p> | 20/07/2017 | n/a | | |

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| | authorisation, including the RMP - Other variation | | | | |
| WS/1092 | <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.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> | 20/07/2017 | 29/06/2018 | SmPC and PL | <p>In study D5553C00003, the combination of dapagliflozin and prolonged release exenatide (a GLP 1 receptor agonist) was compared to dapagliflozin alone and prolonged release exenatide alone in subjects with inadequate glycaemic control on metformin alone (HbA1c \geq 8% and \leq 12%). All treatment groups had a reduction in HbA1c compared to baseline. The combination treatment with dapagliflozin 10 mg and prolonged release exenatide group showed superior reductions in HbA1c from baseline compared to dapagliflozin alone and prolonged release exenatide alone. Combination therapy of dapagliflozin 10 mg and prolonged release exenatide resulted in significantly greater reductions in fasting plasma glucose, in 2 hour post prandial glucose, in body weight and systolic blood pressure at week 28, as compared to either agent alone. These efficacy results were reflected in section 5.1 of the SmPC. In addition the statement that combination with glucagon like peptide 1 (GLP 1) analogues had not been studied, was removed from section 4.4 as result of the availability of this study.</p> |
| PSUSA/10029 /201610 | Periodic Safety Update EU Single assessment - dapagliflozin | 18/05/2017 | 13/07/2017 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10029/201610. |
| WS/1055 | <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.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance</p> | 21/04/2017 | 13/07/2017 | SmPC, Labelling and PL | |

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| | data | | | | |
| A20/0010 | <p>Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 15 April 2016 the PRAC to assess the impact on the benefit-risk balance of canagliflozin containing medicinal products of an increase in amputations, mostly affecting the toes, observed in an ongoing clinical trial (CANVAS) for canagliflozin and a numerical imbalance with regards to amputation events seen in an ongoing renal study CANVAS-R with a similar population as CANVAS.</p> <p>Considering that a class effect cannot be excluded, the European Commission extended on 6 July 2016 the scope of the procedure to include all SGLT2 inhibitors containing medicinal products to allow a review of data from the class.</p> <p>The PRAC was requested to assess the impact thereof on the benefit-risk balance of Invokana, Vokanamet, Forxiga, Edistride, Xigduo, Ebymect, Jardiance and Synjardy and to give its recommendation whether the marketing authorisation of these products should be maintained, varied, suspended or revoked.</p> <p>As the request results from the evaluation of data resulting from pharmacovigilance activities, the CHMP opinion has been adopted on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee.</p> | 09/02/2017 | 20/04/2017 | SmPC and PL | Please refer to the assessment report: SGLT2 inhibitors - EMEA/H/A-20/1442 |

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| WS/0921 | <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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> | 06/04/2017 | n/a | | |
| WS/1056 | <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.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> | 19/01/2017 | 20/04/2017 | SmPC, Labelling and PL | <p>Based on literature data, information on interaction on the interaction between 1,5-anhydroglucitol assay (monitoring glycaemic control method) and the SGLT2 inhibitors was added in section 4.5 of the Summary Product Characteristics as follows:</p> <p>Interference with 1,5-anhydroglucitol (1,5-AG) assay Monitoring glycaemic control with 1,5-AG assay is not recommended as measurements of 1,5-AG are unreliable in assessing glycaemic control in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycaemic control.</p> |
| WS/0968 | <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.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation</p> | 10/11/2016 | n/a | | |
| IAIN/0008 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 25/05/2016 | 20/04/2017 | SmPC and PL | |
| WS/0894/G | This was an application for a group of variations | 14/04/2016 | n/a | | |

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| | <p>following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation</p> <p>B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size</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> | | | | |
| N/0007 | <p>Update of the package leaflet with revised contact details of local the representative for Spain.</p> <p>Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)</p> | 29/03/2016 | | PL | |
| IG/0654 | 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 | 29/02/2016 | n/a | | |
| IG/0653 | 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 | 29/02/2016 | n/a | | |

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| IA/0003 | A.7 - Administrative change - Deletion of manufacturing sites | 28/01/2016 | n/a | | |
| IA/0002 | 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) | 22/12/2015 | n/a | | |
| IG/0633 | 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 | 09/12/2015 | n/a | | |