Veltassa

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
II/0034/G	This was an application for a group of variations. · Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update safety information based on a pooled safety database. The Package Leaflet is updated accordingly. In addition, the MAH took the	25/04/2024	06/06/2024	SmPC and PL	Update of sections 4.4 and 4.8 of the SmPC in order to reflect safety information based on a pooled safety database from study PAT-CR-302 (Diamond). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the PI. These changes do not significantly alter the safety profile of

[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).

	opportunity to implement editorial changes to the SmPC. · Update of section 4.8 of the SmPC in order to add "Hypersensitivity" to the list of adverse drug reactions (ADRs) with frequency "not known", based on post-marketing data. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				patiromer. Overall, the benefit-risk balance of Veltassa, remains positive.
X/0031/G	This was an application for a group of variations. Extension application to introduce a new strength (1 g powder for oral suspension), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of population from 12 to 17 years old for Veltassa based on final results from paediatric study RLY5016-206P (EMERALD); this is a phase 2, open-label, multiple dose study to evaluate the pharmacodynamic effects, safety, and tolerability of patiromer for oral suspension in children and adolescents 2 to less than 18 years of age with chronic kidney disease and hyperkalaemia. As a consequence, sections 1, 2, 4.1, 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 6.5 of the SmPC are updated. The	09/11/2023	05/01/2024	SmPC, Labelling and PL	Please refer to Scientific Discussion "Veltassa EMEA/H/C/004180/X/0031/G".

	Package Leaflet and Labelling are updated in accordance. Version 2.3 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes. Annex I_2.(c) Change or addition of a new strength/potency C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IB/0035/G	This was an application for a group of variations. 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 B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS	31/07/2023	n/a		
IA/0032/G	This was an application for a group of variations. 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 A.7 - Administrative change - Deletion of manufacturing sites 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)	24/02/2023	15/05/2023	Annex II and PL	

	A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites 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 A.7 - Administrative change - Deletion of manufacturing sites				
IA/0033	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	10/02/2023	n/a		
II/0029	Update of sections 4.2 and 4.5 of the SmPC in order to introduce new drug-drug interaction information based on results from four in vitro studies: RLY-TR-0174, titled "In Vitro Evaluation of Potential RLY5016S and Immunosuppressant Drug-Drug Interactions"; RLY-TR-018, titled "In Vitro Evaluation of Potential Drug-Drug Interactions Between Patiromer and Sevelamer Hydrochloride"; "In Vitro Evaluation of Drug-Drug Interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS" and "Drug-drug interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS in a simulated GI tract passage study". The Package Leaflet is updated accordingly.	06/10/2022	15/05/2023	SmPC and PL	This variation concerns the update of the Product Information of Veltassa with the information from four drug-drug interaction studies. Section 4.2 SmPC recommendation remain in place, with only a minor wording amendment. Section 4.5 of the SmPC was updated with a list of medicinal products which did not demonstrate a binding potential in vitro. The advice that administration of patiromer should be separated by at least 3 hours from other oral medicinal products was maintained in the absence of clinical data to support. The MAH has also submitted an amended Package Leaflet to align the information with that in the SmPC. For more information, please refer to the Summary of

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Product Characteristics.
IAIN/0030	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	24/05/2022	15/05/2023	SmPC, Labelling and PL	
R/0028	Renewal of the marketing authorisation.	27/01/2022	24/03/2022	SmPC and Annex II	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Veltassa in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0024	Update of section 4.2 of the SmPC in order to update the posology with information to add the option to use various liquids and soft foods instead of the currently approved options (water, apple, cranberry juice) for preparation of Veltassa oral suspension. This is based on results from a new compatibility study report of Veltassa with juices/liquids and soft foods (REP074062TC). The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/11/2021	24/03/2022	SmPC and PL	Results from a new compatibility study report of Veltassa with juices/liquids and soft foods (REP074062TC) concluded that the following liquids or soft foods can be used to prepare Veltassa oral suspension instead of water : apple juice, cranberry juice, pineapple juice, orange juice, grape juice, pear juice, apricot nectar, peach nectar, yoghurt, milk, thickener, apple sauce, vanilla and chocolate pudding. The mixture should be prepared following the described preparation mode included in the Product information updated accordingly. The potassium content of liquids or soft foods used to prepare the mixture should be considered as part of the dietary recommendations on potassium intake for each individual patient. For more information, please refer to the Summary of Product Characteristics.

IB/0027	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	15/09/2021	n/a		
IA/0026	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	26/08/2021	n/a		
IA/0025/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.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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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	27/07/2021	n/a		

	manufacturer of a novel excipient 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				
IB/0023/G	This was an application for a group of variations. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	20/07/2021	n/a		
PSUSA/10618 /202010	Periodic Safety Update EU Single assessment - patiromer	10/06/2021	n/a		PRAC Recommendation - maintenance
IB/0022	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	09/04/2021	n/a		

IB/0020	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	18/12/2020	n/a		
IA/0019	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	27/11/2020	n/a		
II/0018	Update of section 5.1 of the SmPC in order to update efficacy information based on final results from Study RLY5016-207; this is a randomised, double-blind, placebo-controlled, parallel group study of patiromer to enable concomitant spironolactone treatment in patients with resistant hypertension and CKD. Editorial changes are also made to Section 6.4 of the SmPC. The PI is also brought to the latest QRD version 10.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/10/2020	22/10/2021	SmPC and Annex II	Of the randomized patients, 295 received study treatment (patiromer 147; placebo 148). The primary efficacy endpoint, the proportion of subjects remaining on spironolactone at Week 12, was significantly higher ($p<0.0001$) in the patiromer group (85.7%) compared to the placebo group (66.2%). Significantly more patients received spironolactone 50 mg/day (69.4% versus 51.4%). At Week 12, the mean systolic blood pressure had decreased by 11.0 mmHg (SD 15.34) in the spironolactone + placebo group and by 11.3 mmHg (SD 14.11) in the spironolactone + patiromer group. These decreases from baseline were statistically significant within each treatment group ($p<0.0001$), but not statistically significant between the groups.
PSUSA/10618 /201910	Periodic Safety Update EU Single assessment - patiromer	14/05/2020	n/a		PRAC Recommendation - maintenance
IB/0017	B.I.c.z - Container closure system of the AS - Other variation	11/05/2020	n/a		
IB/0016	B.I.b.1.z - Change in the specification parameters	11/03/2020	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0012/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.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 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.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	17/12/2019	n/a		
IA/0014/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 -	09/12/2019	n/a		

	Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place 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				
IB/0013	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	29/11/2019	n/a		
PSUSA/10618 /201904	Periodic Safety Update EU Single assessment - patiromer	31/10/2019	n/a		PRAC Recommendation - maintenance
IB/0010/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	03/07/2019	n/a		

	changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data				
II/0007	Update of section 4.2, and 5.1 of the SmPC to reflect the results of study RLY5016-401: an open-label, randomised, parallel group phase 4 study of the efficacy and safety of patiromer for oral suspension with or without food for the treatment of hyperkalemia (TOURMALINE). The PL has been updated accordingly. Section 4.5 was also updated to update information on the effect of patiromer on other medicinal products. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/05/2019	06/06/2019	SmPC and PL	In the TOURMALINE open-label study, 114 patients with hyperkalaemia were randomized to patiromer once daily with food or without food. Serum potassium at the end of treatment, the change from baseline in serum potassium, and the mean dose of patiromer were similar between groups. Veltassa can therefore be taken with or without food. Section 5.1 and 4.2 of the SmPC were updated accordingly. For completeness the percentage of patients receiving RAAS inhibitor therapy with CKD, diabetes mellitus and heart failure from phase 2 and 3 clinical studies has been included in section 5.1 of the SmPC. Section 4.5 was updated to reflect that as patiromer is not absorbed or metabolised by the body, there are limited effects on the function of other medicinal products.
PSUSA/10618 /201810	Periodic Safety Update EU Single assessment - patiromer	16/05/2019	n/a		PRAC Recommendation - maintenance
IB/0008/G	This was an application for a group of variations.	04/01/2019	n/a		

	B.I.a.z - Change in manufacture of the AS - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits				
PSUSA/10618 /201804	Periodic Safety Update EU Single assessment - patiromer	31/10/2018	n/a		PRAC Recommendation - maintenance
IB/0006	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	10/09/2018	n/a		
IA/0004/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test 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)	18/07/2018	n/a		
PSUSA/10618 /201710	Periodic Safety Update EU Single assessment - patiromer	17/05/2018	n/a		PRAC Recommendation - maintenance

IA/0003/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	11/04/2018	n/a		
IAIN/0001/G	This was an application for a group of variations. 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 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) B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	16/11/2017	n/a		