Velphoro

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/0027/G	This was an application for a group of variations. 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	25/03/2022	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).

	starting material/reagent/intermediate - Minor changes to an approved test procedure 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				
IA/0026/G	This was an application for a group of variations. B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	07/03/2022	n/a		
IB/0023	In addition the MAH has also taken this chance to make updates to Annex A for Danish, Dutch, Italian, Norwegian, German, Greek, Spanish, Estonian, Finnish, French, Croatian, Lithuanian, Latvian, Polish, Romanian and Swedish to bring them in line with the	11/01/2022		SmPC, Labelling and PL	

	correct EN. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
IA/0024/G	This was an application for a group of variations. B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.3.b - Change in test procedure for the immediate packaging of the finished product - Other changes to a test procedure (including replacement or addition) B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	10/01/2022	n/a		
IB/0022/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.g.5.b - Implementation of changes foreseen in an approved change management protocol - Requires further supporting data	10/11/2021	n/a		
X/0020/G	This was an application for a group of variations. Extension of indication to add indication to use Velphoro for the control of serum phosphorus levels	17/09/2020	16/11/2020	SmPC, Annex II, Labelling and PL	Please refer to the scientific discussion: Velphoro EMEA/H/C/002705/X/0020/G

	in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/1.73 m2) or with CKD on dialysis, based on the results from an open-label, randomised, active-controlled, parallel group, multicentre, phase 3 study investigating the safety and efficacy of Velphoro and calcium acetate in paediatric and adolescent CKD patients with hyperphosphataemia (Study PA-CL-PED-01). As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 9.0 is also agreed. Furthermore, the PI is brought in line with the latest QRD template version 10.1. Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0021	Update of section 5.1 of the SmPC in order to add information related to the results of the VERIFIE study. This was a non-interventional voluntary PASS trial, which aimed to investigate the short and long-term real-life safety, effectiveness, and adherence of	14/05/2020	16/11/2020	SmPC	The SmPC section 5.1 is updated with post-authorisation data in adult patients on haemodialysis (n=1,198) or peritoneal dialysis (n=160), who were followed in routine clinical practice for 12 to 36 months (safety analysis set, N=1,365). In the safety analysis set, the most common

	Velphoro in patients with CKD and hyperphosphatemia undergoing haemodialysis or peritoneal dialysis. It was listed as an additional pharmacovigilance activity (EMEA/H/C/002705/MEA/002), a category 3 study in the RMP. Furthermore, minor editorial wording changes in section 4.2 to provide consistent information between the SmPC and that already existing in the Labelling and PL were introduced. The applicant took also the opportunity to implement minor editorial change to the labelling. The RMP 8.1 has also been submitted. In addition, the RMP is converted to the RMP template Revision 2. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1. The requested variation proposed amendments to the Summary of Product Characteristics and to the Risk Management Plan (RMP). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				ADRs were diarrhoea and discoloured faeces, reported by 14% (n=194) and 9% (n=128) of patients, respectively. The incidence of diarrhoea was highest in the first week and decreased with duration of use. Diarrhoea was of mild to moderate intensity in most patients and resolved in the majority of patients within 2 weeks. Discoloured (black) faeces is expected for an oral iron-based compound and may visually mask gastrointestinal bleeding. For 4 of the 40 documented concomitant gastrointestinal bleeding events, Velphoro-related stool discolouration was reported as causing an insignificant delay in diagnosis of gastrointestinal bleeding, without affecting patient health. In the remaining cases, no delay in diagnosis of gastrointestinal bleeding has been reported. The results from this study showed that the effectiveness of Velphoro in a real-life setting (including concomitant use of other phosphate binders in 45% of patients), was in line with that observed in the phase 3 clinical study. The RMP summary of safety concerns is revised to remove the important identified risks of Diarrhoea, Potential Iron Accumulation and Masking of Potential GI Bleeding Due to Velphoro-Induced Discoloured (Black) Faeces and to remove the missing information of Long term use beyond 1 year, Use in patient population receiving Velphoro concomitantly with other PBs and Use in PD patients. The completed paediatric study PA-CL-PED-01 is removed from the list of additional pharmacovigilance activities.
PSUSA/10296 /201811	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	14/06/2019	n/a		PRAC Recommendation - maintenance

R/0018	Renewal of the marketing authorisation.	31/01/2019	25/03/2019	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Velphoro in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10296 /201805	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	17/01/2019	n/a		PRAC Recommendation - maintenance
PSUSA/10296 /201711	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	14/06/2018	n/a		PRAC Recommendation - maintenance
IB/0016	B.I.d.1.a.1 - Stability of AS - Change in the re-test period/storage period - Reduction	24/04/2018	n/a		
IB/0014	B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)	20/02/2018	18/10/2018	SmPC, Labelling and PL	
PSUSA/10296 /201705	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	11/01/2018	n/a		PRAC Recommendation - maintenance
IA/0013	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)	30/11/2017	n/a		
II/0012	Update of section 4.4 of the SmPC in order to remove a warning related to allergy to gluten. The Package Leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor corrections in	16/11/2017	18/10/2018	SmPC, Labelling and PL	

	the SmPC in line with the Company Core Data Sheet (CCDS). Moreover, the MAH took the opportunity to bring the Annex IIIA in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10296 /201611	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	09/06/2017	n/a		PRAC Recommendation - maintenance
II/0009/G	This was an application for a group of variations. B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP	23/02/2017	n/a		
PSUSA/10296 /201605	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0007/G	This was an application for a group of variations.	01/09/2016	26/07/2017	SmPC, Annex II, Labelling	

	A.1 - Administrative change - Change in the name and/or address of the MAH 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.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)			and PL	
PSUSA/10296 /201511	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	09/06/2016	n/a		PRAC Recommendation - maintenance
PSUSA/10296 /201505	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	14/01/2016	n/a		PRAC Recommendation - maintenance
II/0004/G	This was an application for a group of variations. 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	17/09/2015	09/09/2016	SmPC and Annex II	
PSUSA/10296 /201502	Periodic Safety Update EU Single assessment - sucroferric oxyhydroxide	10/09/2015	n/a		PRAC Recommendation - maintenance

IB/0002	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/01/2015	n/a		
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/11/2014	09/09/2016	Labelling and PL	