VIFOR PHARMA

Norman Stockbridge, MD., Ph.D.
Division of Cardiology and Nephrology
FDA/Center for Drug Evaluation and Research (CDER)
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-12667

DATE 26 November 2021,

SUBJECT

NDA 205739 / Serial 0160
Veltassa® (patiromer) for Oral Suspension

RESPONSE TO PREA NON-COMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

Dear Dr Stockbridge,

Reference is made to the New Drug Application (NDA 205739) for Veltassa® (patiromer) Powder for Oral Suspension, 8.4 g, 16.8 g and 25.2 g indicated for the treatment of hyperkalemia. Additional reference is made to the Post Marketing Requirements (PMRs):

PMR-2980-1 Study 1: A Phase 2, Open-Label, Multiple Dose Study to Evaluate the Pharmacodynamic Effects, Safety, and Tolerability of Veltassa (Patiromer Sorbitex Calcium) for Oral Suspension in Children and Adolescents 2 to 18 Years of Age with Hyperkalemia

Final Protocol Submission:	03/2016
Study Completion:	12/2020
Final Report Submission:	09/2021

PMR-2980-2 Study 2: A Phase 2, Open-Label, Multiple Dose Study to Evaluate the Pharmacodynamic Effects, Safety, and Tolerability of Veltassa (Patiromer Sorbitex Calcium) for Oral Suspension in Infants and Toddlers Under 2 Years of Age with Hyperkalemia

CONTACT

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Final Protocol Submission:	03/2020
Study Completion:	11/2024
Final Report Submission:	07/2025

The purpose of this letter is to respond to FDA's notification of Non-Compliance with PREA letter for PMR-2980-1 dated October 15, 2021.

Background:
The study protocol for study RLY5016-206p (also known as the EMERALD study) intended to address PMR 2980-1 was submitted to IND (b) (4) on 14 March 2016 (SN0099) and the first patient was enrolled in on 6 July 2017. Up to 54 subjects were planned to be enrolled in the study in three sequentially enrolled different aged cohorts (Cohort 1: 12 to <18 years; Cohort 2: 6 to <12 years; and Cohort 3: 2 to <6 years). Cohort 1 was completed with 14 subjects and enrollment commenced for Cohort 2 in July 2019. Cohort 2 has recruited a total of 9 (out of planned 12) subjects enrolled. No subjects 2 to <6 years have been recruited.

Vifor submitted a request (b) (4) n response (General Advice dated September 27, 2021), the Agency did not support Vifor's request due to concerns that this may result in additional delays obtaining the data needed to expand the indication to patients 2 to <6 years of age. In addition, Vifor were advised to submit the proposed amendments to PMRS 2980-1 and 2980-2 and goal dates as a formal "Request for Deferral Extension of Required Pediatric Assessments" to the subject NDA.

REQUEST FOR DEFERRAL EXTENSION OF REQUIRED PEDIATRIC ASSESSMENTS
Vifor acknowledges and regrets the delay in meeting our PREA commitments within the required timeframe. Despite effort by the sponsor to progress and maintain the EMERALD study per the agreed PMR 2980-1 schedule, enrollment in this already very limited patient population has been significantly impacted by multiple factors such as:

- Unanticipated delays due to the global Covid-19 pandemic and subsequent lockdowns and restrictions at study sites impacted completion of enrollment of Cohort 2.
- Complex study design (particularly with respect to the number of visits per protocol relative to standard of care) placing additional burden on patients/parents and overall willingness to enroll. This was further exacerbated by the Covid-19 pandemic and country lockdowns.
- Although selected because of having considerable experience in pediatric development; Vifor's contracted contract research organization (CRO) does not have specific expertise or a dedicated referral function to overcome enrollment challenges in this pediatric hyperkalemia population. The CRO also has a limited global footprint and is unable to open enrollment in countries where faster enrollment may be feasible.

- Delayed overall completion of PMR 2980-1 due to sequential Cohort enrollment has had consequence on the plan and schedule for PMR 2980-2.

Vifor is committed to fulfilling our PREA requirements with diligence and will promptly resume efforts to enroll the EMERALD study and progress future study (b) (4) which will fulfill PMR 2980-2.

Consistent with the Agency's General Advice dated September 27, 2021, Vifor will now plan to submit to the IND the available data from the EMERALD in ages 6 to <18 (Cohorts 1 and 2) for the Agency's review by March 2022. In addition, subject to evaluation by Independent Data Safety Monitoring Committee, enrollment into Cohort 3 for ages 2 to <6 years will commence. Vifor will incorporate the advice received into the protocol(s) design that may reduce complexity and facilitate enrollment in the countries where EMERALD is currently open.

Due to the specific operational issues with the contracted CRO noted above and the ongoing Covid-19 pandemic, these actions may not be sufficient to secure the appropriate number of subjects required to fulfil both PREA PMRs in a timely fashion. Vifor therefore plan to progress development of the (b) (4) study protocol (b) (4) . This plan for study (b) (4) Vifor therefore propose revision to PMR-2980-2 (b) (4)

In conclusion, we hereby formally request a deferral extension of our PREA commitment as follows (**bold** type to note changes):

PMR-2980-1 Study 1: A Phase 2, Open-Label, Multiple Dose Study to Evaluate the Pharmacodynamic Effects, Safety, and Tolerability of Veltassa (Patiromer Sorbitex Calcium) for Oral Suspension in Children and Adolescents 2 to 18 Years of Age with Hyperkalemia

Final Protocol Submission: (b) (4)	03/2016
Study Completion:	**06/2024**
Final Report Submission:	**03/2025**

PMR-2980-2 Study 2: A Phase 2, Open-Label, Multiple Dose Study to Evaluate the Pharmacodynamic Effects, Safety, and Tolerability of Veltassa (Patiromer Sorbitex Calcium) for Oral Suspension (b) (4) with Hyperkalemia

(b) (4)	(b) (4)
Final Protocol Submission:	**07/2022**
Study Completion:	**12/2026**
Final Report Submission:	**09/2027**

Vifor respectfully requests that public posting of the FDA Notification of Non-Compliance with PREA for PMR-2980-1 and our response letter be deferred so that this request for deferral extension can be evaluated. We understand that should our deferral extension not be accepted both will be posted publicly in accordance with section 505B(d)(1) of the Federal FD&C act. Vifor requests in this case that FDA make appropriate redactions for trade secrets and confidential commercial information.

Should you have any questions or require information related to this submission, please contact me by telephone or email as indicated.

This documentation has been submitted electronically via eCTD to the FDA ESG. All files were scanned with the most recent version of Windows Defender Antivirus and are virus-free. For any technical issues regarding this electronic submission, please contact Mr. Robert Selak, Regulatory Affairs Operations Specialist, Vifor Pharma, at +41 58 8518 598, or robert.selak@viforpharma.com.

Yours sincerely,
Vifor Pharma, Inc.

Alexandra Park