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ESG

**RESPONSE TO PREA NON-COMPLIANCE LETTER**

Dragos Roman, MD, Director
Division of Gastroenterology and Inborn Errors Products (DGIEP)
Office of Drug Evaluation III
Food and Drug Administration
Center for Drug Evaluation and Research
Attn: Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

**RE: NDA 021361: XIFAXAN® (rifaximin) Tablets, 200 mg and 550 mg**
**Sequence 0105: Postmarketing Requirements – Response to PREA Non-Compliance Letter of August 21, 2019**

Dear Dr. Roman:

Reference is made to Salix Pharmaceuticals, Inc. and NDA 021361, XIFAXAN® (rifaximin) Tablets, 200 mg and 550 mg for the treatment of travelers' diarrhea (TD); reduction in risk of overt hepatic encephalopathy (HE) recurrence; and the treatment of irritable bowel syndrome with diarrhea (IBS-D).

Reference is made to the following Pediatric Research Equity Act (PREA) Post Marketing Requirement (PMR) (Reference ID 3766565):

- PMR 2900-1: Conduct a pharmacokinetic, pharmacodynamics, tolerability and dose ranging study in subjects 6 years through 17 years, to assess safety and to determine the doses to be used in the efficacy study. Age-specific endpoints, i.e. a clinical outcome assessment utilizing Patient Reported Outcomes (PROs) or a PRO instrument to evaluate efficacy of rifaximin for the treatment of irritable bowel disease (IBS) in children, should be developed.

Reference is also made to the FDA Notification of Non-Compliance with PREA letter dated August 21, 2019 (Reference 4480185) stating the failure to meet the (PMR) for this application because you have not yet submitted your pediatric assessment for PMR 2900-1, which was

deferred until March 31, 2019.

Reference is further made to the Deferral Extension Requested submission (Sequence 0095) and Response to FDA Request for Information (Sequence 0097) informing the Agency of the progress made to satisfy PMR 2900-1.

As requested the Sponsor provides the proposed pharmacokinetic (PK) study (protocol (b) (4) which also includes a (b) (4) with supporting rationale for FDA review and feedback in Module 1.17.2.

The Sponsor also provides the following draft study reports used to provide the dosing rationale in protocol (b) (4) in Module 4.2.2.1:

- Draft Study Report (b) (4)
- Draft Study Report

The Sponsor notes that protocol (b) (4) and final study reports (b) (4) will be submitted to the IND 071425.

This submission is provided in electronic Common Technical Document (eCTD) format and is approximately 1 MB in size. The content of the submission has been verified to be free of viruses using the latest version of Carbon Black Defense. The submission is being provided via the FDA's Electronic Submission Gateway (ESG). Please note that a letter of non-repudiation dated January 13, 2015 is on file with the Agency.

The information contained in this submission is confidential and as such should be handled in accordance with the provisions established in 21 CFR § 314.430.

Should you have any questions or comments regarding this submission, please do not hesitate to contact me. Alternatively, you may contact Libette Luce, MA, Senior Director, Global Regulatory Affairs at 908-541-3425 or by email at libette.luce@bauschhealth.com

Sincerely,

Timothy Ebert

Digitally signed by Timothy Ebert
DN: dc=vrx, dc=Corp, dc=Valeant, ou=North America, ou=Bridgewater, ou=Users, ou=Employees, cn=Timothy Ebert
Date: 2019.10.03 13:18:36 -04'00'

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APPEARS THIS WAY ON ORIGINAL