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ESG

RESPONSE TO PREA NON-COMPLIANCE

Tiffany R. Farchione, MD, Director
Division of Psychiatry Products (DPP)
Office of Drug Evaluation I
Center for Drug Evaluation and Research
Food and Drug Administration
Attn: Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: NDA 022108: **APLENZIN® (buproprion hydrobromide) Extended-Release Tablets Sequence 0075: Postmarketing Requirements – Response to PREA Non-Compliance & Deferral Extension Requested**

Dear Dr. Farchione:

Referenced is made to New Drug Application (NDA) 022108, APLENZIN® (bupropion hydrobromide) Extended Release Tablets, 174, 348 and 522 mg for the treatment of major depressive disorder (MDD) and seasonal affective disorder (SAD).

Reference is made to the following Pediatric Research Equity Act (PREA) Post Marketing Requirements (PMR) (Reference ID: 4405873):

PMR 133-1: Deferred pediatric study under PREA for the treatment of Major Depressive Disorder in pediatric patients ages 7 to 17.

Reference is also made to the FDA Notification of Non-Compliance with PREA letter dated March 19, 2018 requesting formal response for reason(s) for the delayed pediatric assessment and a date by which you expect to submit the assessment. A request for deferral extension was also provided as an option to the sponsor (Reference ID: 4405873).

The sponsor would like to formally provide a PMR proposal, justification for timeline extension and request for deferral extension with this submission.

PMR Proposal and Justification for Timeline Extension

The sponsor acknowledges the missed milestone date of which the pediatric assessment was to be provided to FDA. The sponsor faced manufacturing challenges with the selected pediatric dosage form of bupropion hydrobromide (b) (4). (b) (4)

(b) (4)

The sponsor submitted final clinical study report V01-033-106 to FDA on February 6, 2019 and asked for confirmation if the (b) (4) dosage (b) (4) could be used in the pediatric efficacy trial (b) (4) On April 2, 2019 the sponsor received FDA correspondence via email from Kofi Ansah, PharmD, MS, MBA, Senior Regulatory Health Project Manager, that the sponsor may proceed with the efficacy trial. FDA further advised the sponsor to be aware that any future labeling will reflect the way the doses were given in the trial (b) (4)

As concurrence has been reached between the sponsor and FDA on the use of the pediatric dosage form of bupropion hydrobromide (b) (4) the efficacy study may proceed. The sponsor is currently reviewing protocol (b) (4), which was submitted to FDA for review on May 2, 2014 (IND 073781; Sequence 0019) and revising the document for administrative and formatting changes. The sponsor is also onboarding a contract research organization (CRO) specializing in pediatric psychology studies who will conduct the study for the sponsor. The CRO will be ready to begin to support and conduct the study in January 2020.

Additionally, the sponsor is preparing for the manufacture (b) (4) for use in study V01-BUPA-401. The (b) (4) projected to be ready for the study in January 2020.

Deferral Extension Requested

The sponsor proposes the revise PREA PMR timelines:

Original Timeline	Proposed Timeline
Final Report Submission: 02/28/2019	Final Protocol Submission: 07/31/2019 Study Completion: 01/31/2024 Final Report Submission: 06/30/2024

The sponsor continues to work toward a successful efficacy study in pediatric patients whereby safety of the pediatric population remains the highest priority. The sponsor would like to formally request a deferral extension based on the proposed revised timelines and clinical plan provided with this submission.

The sponsor looks forward to working with the Division to obtain agreement on the PREA PMR study program.

This submission is provided in electronic Common Technical Document (eCTD) format and is approximately 2 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 § 312.130.

Should you have any questions or comments regarding this submission, please do not hesitate to contact me. Alternatively, you may contact Isabelle B. Lefebvre, MSc.RA, (RAC EU & US), Vice President, Global Regulatory Affairs at 908-541-3065 or by email at isabelle.lefebvre@bauschhealth.com.

Sincerely,

Libette Luce

Digitally signed by Libette Luce
DN: dc=vrx, dc=Corp, dc=Valeant, ou=North America, ou=Bridgewater, ou=Users, ou=Employees, cn=Libette Luce
Date: 2019.04.17 15:24:15 -04'00'

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