Forest Research Institute, Inc.
A Subsidiary of Forest Laboratories, Inc.
Harborside Financial Center ♦ Plaza V, Suite 1900 ♦ Jersey City, NJ 07311 ♦ P: (201) 427-8550 ♦ F: (631) 858-7921

August 6, 2014

Robert Rappaport, MD
Director
Division of Anesthetic, Analgesia, and Addiction Products (DAAAP)
Center for Drugs Evaluation and Research
Food and Drug Administration
5901-8 Ammendale Road
Beltsville, MD 20707-1266

NDA: 21-359 - Rectiv® (nitroglycerin)
IND: (b) (4) – Rectiv® (nitroglycerin)
RE: Response to PREA Non-Compliance Letter dated June 25, 2014
Sequence No.: 0002 / 0107

Dear Dr. Rappaport:

Reference is made to NDA 021-359 for Rectiv® (nitroglycerin) Ointment 0.4% approved on June 21, 2011 for the treatment of moderate to severe pain associated with chronic anal fissures and to the Postmarketing Requirements 1791-1 and 1791-3. Reference is also made to the FDA's Notification of Non-Compliance with PREA Letter dated June 25, 2014 regarding the submission of the pediatric assessment for PMR 1791-1. The submission deadline for the final clinical study report for study APT-NIT_S-PRO-M_PEDKPK1_E01, which was intended to fulfill PMR 1791-1, outlined in the Approval Letter for Rectiv® was December 2013.

The purpose of this submission is to respond to the Notification of Non-Compliance Letter within the requested 45 calendar days. Reference is also made to the Request for Release of Pediatric Study Requirements, PMR 1791-1 and PMR 1791-3 submitted on August 5, 2014 (Sequence No.: 0001).

This NDA was approved by FDA on June 21, 2011 when Prostrakan Inc., was the NDA sponsor. In January 2012, the NDA 021359 for Rectiv®, was transferred to Aptalis Pharma US Inc., who obtained exclusive marketing rights for Rectiv® in the US. In a Type C Meeting request submitted in September 2012, Aptalis requested a waiver for the three post marketing requirements for clinical studies in children < 12 years old (PMR 1791-2, 1791-4, and 1791-5) and a deferral extension for the two post marketing requirements for clinical studies in patients aged ≥ 12 to < 17 years (PMR 1791-1 and 1791-3). In February 2014, Forest Laboratories, Inc. acquired Aptalis as well as the responsibility for all post-marketing requirements for Rectiv®.

On June 17, 2014, FDA granted the release of the post marketing requirement for studies in children < 12 years old (1791-2, 1791-4, and 1791-5). No formal response to the proposed deferral timeframe was received from the Division regarding PMR1791-1 and PMR1791-3 prior to the receipt of a Notification of Non-Compliance with PREA dated June 25, 2014 for PMR1791-1.

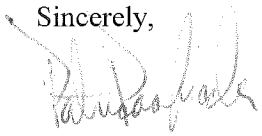
To address the remaining requirements outlined in the June 21, 2011 approval letter, for which Aptalis had requested a deferral, Forest submitted a request for release from the requirement to conduct the remaining studies fulfilling PMR 1791-1 and 1791-3 on August 5, 2014 (Sequence No.: 0001) due to the low prevalence of chronic anal fissures requiring treatment for moderate to severe pain in the adolescent population and our ability to enroll patients.

Forest Research Institute, Inc.
A Subsidiary of Forest Laboratories, Inc.
Harborside Financial Center ♦ Plaza V, Suite 1900 ♦ Jersey City, NJ 07311 ♦ P: (201) 427-8550 ♦ F: (631) 858-7921

The lack of patient enrollment in the study has been attributed to the extremely small population of adolescent patients requiring treatment for moderate to severe pain associated with chronic anal fissure, making it unfeasible to identify and recruit patients into the clinical trial. This assessment is supported by a recent community-based retrospective study which suggested that the incidence of chronic anal fissures in the 12-17 year old age group is as low as the <12 year old age group. (Mapel D et al, 2014). In view of the fact that the FDA sought fit to grant a waiver for the Rectiv® PMR studies in pediatric patients < 12 years of age in part due to the low prevalence of the condition and need for treatment in that population, Forest considers the comparably low prevalence in the 12-17 year age range to provide similar basis for a such a waiver in this age range.

If you have any questions about this submission, please contact me at (201) 427-8402 or, in my absence, Kathleen Waldron, MBA, at (201) 386-2115.

Sincerely,



Patricia Pacificador, PharmD
Senior Manager, Regulatory Affairs
Patricia.Pacificador@frx.com

cc: Christopher Hilfiger, Regulatory Project Manager
Division of Anesthesia, Analgesia, and Addiction Products