DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021107/S-014

SUPPLEMENT APPROVAL

Prometheus Laboratories, Inc.
Attention: David Furlano, Ph.D.
Vice President, Regulatory Affairs and Quality Systems
9410 Carroll Park Drive
San Diego, CA 92121

Dear Dr. Furlano,

Please refer to your supplemental new drug application (NDA) dated September 19, 2008, received September 22, 2008, submitted under section505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lotronex (alosetron hydrochloride) Tablets, 0.5mg and 1mg.

This supplemental application provides for a proposed risk evaluation and mitigation strategy (REMS) for Lotronex (alosetron hydrochloride) Tablets and was submitted in accordance with section 909(b)(1) of the Food and Drug Administration Amendments Act of 2007 (FDAAA). Under section 909(b)(1) of FDAAA, we identified Lotronex (alosetron hydrochloride) Tablets as a product deemed to have in effect an approved REMS because there were in effect on the effective date of FDAAA, March 25, 2008, elements to assure safe use required under 21 CFR 314.520.

We also refer to your submissions dated September 29, 2008; December 18, 2008; February 13, 2009; May 8, 2009; September 30, 2009; December 3, 4, 14 and 17, 2009; April 14, 2010; July 21, 2010; and August 3 and 5, 2010.

In accordance with section 505-1 of the FDCA, we have determined that a REMS is necessary for Lotronex (alosetron hydrochloride) Tablets to ensure the benefits of the drug outweigh the risk of ischemic colitis and serious complications of constipation. Your proposed REMS, as amended and appended to this letter, is approved. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

In addition, we note that NDA 021107 is approved under the provisions of 21 CFR 314.520 (Subpart H).

The REMS assessment plan should include, but is not limited to, the following information:

a. The number of certified prescribers in the Prescribing Program for Lotronex (alosetron hydrochloride) Tablets that have undergone certification during the reporting period and cumulatively.

b. The number of prescribers who are removed from enrollment in the Prescribing Program for Lotronex (alosetron hydrochloride) Tablets during the reporting period due to noncompliance.

c. The number of prescribers not enrolled in the Prescribing Program for Lotronex (alosetron hydrochloride) Tablets who are writing prescriptions for Lotronex (alosetron hydrochloride) Tablets and whether pharmacists are filling prescriptions written by prescribers not enrolled in the Prescribing Program for Lotronex (alosetron hydrochloride) Tablets.

d. Corrective and preventative actions taken to address non-compliance with distribution and dispensing requirements during the reporting period and cumulatively.

e. Lotronex (alosetron hydrochloride) Tablets drug use patterns during the reporting period and cumulatively, to include reasons for use, patient demographics, and prescribing medical specialists.

f. The number of cases of ischemic colitis, ischemic colitis involving ischemic changes, ischemia, or necrosis of the colon; constipation requiring hospitalization or emergency room visit; possible complications of constipation such as obstruction, perforation, intestinal ulceration, toxic megacolon, ileus or impaction resulting in hospitalization or emergency room visit; and all reports of death, regardless of causality, during the reporting period and cumulatively.

g. The narrative summary, tabular analyses and discussion of the above cases (in "f.") received during the reporting period including the clinical significance of these events.

h. An evaluation of prescribers, pharmacists, and patients' understanding of the serious risks of Lotronex (alosetron hydrochloride) Tablets. Results of surveys of physicians', patients', and pharmacists' understanding of the serious risks of Lotronex (alosetron hydrochloride) Tablets are due with the second REMS assessment, at 12 months, and all subsequent REMS assessments.

i. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.

j. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(A), an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

Assessments of an approved REMS must also include, under sections 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report

required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of FDCA.

Prominently identify future submissions containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 021107 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021107
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021107
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

As part of the approval under Subpart H, as required by 21 CFR 314.550 you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days before the intended time of initial distribution of the labeling or initial publication of the advertisement. Send one copy to the Division of Gastroenterology and two copies of the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least

24 hours prior to issuing the letter, an electronic copy of the letter to this NDA and to CDERMedWatchSafetyAlerts@fda.hhs.gov, and a paper copy to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave.
Building 32, Mail Stop 5353
Silver Spring, MD 20993

If you have any questions, call Diane Munro, Regulatory Project Manager at (301) 796-4257.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology Products
Office of Drug Evaluation III

Attachments:
Labeling
REMS Document
REMS Materials

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21107	SUPPL-14	PROMETHEUS LABORATORIES INC	LOTRONEX

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOYCE A KORVICK
09/02/2010