DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 200652/S-004

SUPPLEMENT APPROVAL

Roxane Laboratories, Inc.
c/o West-Ward Pharmaceuticals Corp.
Attention: Sarah A. Smith
Director, Drug Regulatory Affairs and Labeling
1809 Wilson Road
Columbus, Ohio 43228

Dear Ms. Smith:

Please refer to your Supplemental Abbreviated New Drug Application (sANDA) dated and received September 23, 2016, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) Alosetron Hydrochloride Tablets, 0.5 mg and 1.0 mg.

We acknowledge receipt of your amendment dated November 4, 2016.

This supplemental abbreviated new drug application provides for modifications to the approved Alosetron Hydrochloride risk evaluation and mitigation strategy (REMS).

APPROVAL

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Alosetron Hydrochloride was originally approved on May 4, 2015. The most recent modification was approved on March 24, 2016. The REMS consists of elements to assure safe use (ETASU). Your proposed modification to the REMS consists of changes to reflect the inclusion of an additional ANDA into the alosetron REMS.

Your proposed modified REMS, amended on November 4, 2016, and appended to this letter, is approved.

Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines that an assessment is needed to evaluate whether the approved strategy should be modified to ensure the benefits of the drug outweigh the risks of the drug or to minimize the burden on the health care delivery system of complying with the REMS.

Additionally, the details for what should be included in your REMS assessments and the dates of the REMS assessments are listed in Appendix 1.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

ANDA 200652 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

We remind you that in addition to the REMS assessments submitted according to the dates listed in Appendix 1, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of FD&C Act prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing a proposed modification of the REMS or any REMS assessments with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

ANDA 200652 REMS ASSESSMENT

NEW SUPPLEMENT FOR ANDA 200652/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 200652/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR ANDA 200652/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES SUBMITTED IN SUPPLEMENT XXX

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission.

REMS REVISIONS FOR ANDA 200652

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

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

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

If you have any questions, call CDR Stacy Barley, REMS Coordinator, at (301) 796-2137.

Sincerely,

{See appended electronic signature page}
Trueman W. Sharp, M.D., M.P.H.
Acting Deputy Director
Office of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):
Appendix 1
REMS

Appendix 1

Dates for submission of waiver-granted REMS assessments

Roxane will submit REMS Assessments to FDA 18 months following the REMS modification approval on January 7, 2016, and every 12 months thereafter. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Roxane will submit each assessment so that it will be received by the FDA on or before the due date.

REMS Assessment Plan

The REMS Assessment Plan includes, but is not limited to, the following:

1. Results of an evaluation of whether patients received counseling from the prescriber, the patients' understanding of the serious risks of ischemic colitis and serious complications of constipation associated with alosetron, and the actions patients need to take should they experience early warning signs and symptoms of these risks.
2. Results of an evaluation of prescriber understanding of the appropriate patient population, the risks of ischemic colitis and serious complications of constipation associated with alosetron, and the importance of counseling patients about these risks. The evaluation will include a comparison of prescribers who completed training and prescribers who have not reported completion of training.
3. The number of prescribers and medical specialty of prescribers who reported that they completed training in the Alosetron REMS Program, including the number and medical specialty of prescribers contacted by Roxane to become trained after prescribing alosetron and the number and medical specialty contacted who completed training, during the reporting period and cumulative.
4. The number of prescribers who have not completed training and are writing prescriptions.
5. Numbers of prescriptions, by year for the last five years and annually thereafter.
6. Number of cases of the following events reported (from any source) during the reporting period and cumulative:
    - All reports of ischemic colitis;
    - All reports involving ischemic changes, ischemia, or necrosis of the colon
    - All reports involving constipation requiring hospitalization or emergency room visit;
    - All reports involving possible complications of constipation such as obstruction, perforation, intestinal ulceration, toxic megacolon, ileus, or impaction resulting in hospitalization or emergency room visit;
    - All reports of death, regardless of causality.
7. Summary and discussion of the above cases (received during the reporting period) and the clinical significance of these events.
8. An assessment of the extent to which the elements to assure safe use are meeting the goals or whether the goals or such elements should be modified.

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

/s/

TRUEMAN W SHARP
11/22/2016