DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-361

Salix Pharmaceuticals, Inc.
Attention: Mr. David Kashiwase
3600 West Bayshore Road
Suite 250
Palo Alto, CA 94303

Dear Mr. Kashiwase:

Please refer to your new drug application (NDA) dated December 21, 2001, received December 26, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xifaxan™ (rifaximin) Tablets 200 mg.

We acknowledge receipt of your submissions dated:

October 30, 2002
May 2, 2003
October 7, 2003
October 31, 2003
November 24, 2003
November 25, 2003 (2)
December 9, 2003
January 20, 2004
February 5, 2004
February 25, 2004
March 17, 2004
April 12, 2004
April 21, 2004
April 22, 2004
April 26, 2004
April 29, 2004
May 4, 2004
May 12, 2004
May 17, 2004
May 19, 2004
May 21, 2004

The November 25, 2003 submission constituted a complete response to our October 25, 2002 action letter.

This new drug application provides for the use of Xifaxan™ (rifaximin) Tablets 200 mg for the following indication:

> Xifaxan™ Tablets are indicated for the treatment of patients (≥ 12 years of age) with travelers' diarrhea caused by noninvasive strains of *Escherichia coli*.
>
> Xifaxan™ Tablets should not be used in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than *Escherichia coli.*

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert) and submitted labeling (immediate container and carton labels) submitted May 21, 2004. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-361**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages 0 to 3 years and deferring pediatric studies for ages 3 years to 12 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The statuses of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

1. Deferred pediatric studies under PREA for the treatment of travelers' diarrhea in pediatric patients ages 3 years to 12 years.

   Final Report Submission: May 1, 2009

Submit final study reports to this NDA. For administrative purposes, all submissions related to these pediatric postmarketing study commitments must be clearly designated "**Required Pediatric Study Commitments**".

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Special Pathogen and Immunologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Andrei Nabakowski, Pharm.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Mark Goldberger, M.D., M.P.H.
Director
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosures(2): Xifaxan™ Package Insert
Xifaxan™ Patient Package Insert

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

/s/

Edward Cox
5/25/04 06:04:48 PM
for Mark J. Goldberger, M.D., M.P.H.