DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-468/S-004
NDA 21-468/S-005

Dennis Ahern, M.S.
Associate Director, Regulatory Affairs
Shire US, Inc.
725 Chesterbrook Blvd.
Wayne, PA 19087-5637

Dear Mr. Ahern:

Please refer to your supplemental new drug application (S-005) dated September 29, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for FOSRENOL® (Lanthanum Carbonate) Chewable Tablets, 250 and 500mg.

Please also refer to the approval letter for S-004 dated November 23, 2005 for the new formulation of FOSRENOL® (Lanthanum Carbonate) Chewable Tablets, 250, 500, 750, and 1000 mg.

We acknowledge receipt of your submissions dated November 29, 2005 (NDA 21-468/S-005) and December 9, 2005 (NDA 21-468/S-004).

NDA 21-468/S-005 "Changes Being Effected" supplemental new drug application provides for revisions to the labeling to include a precautionary statement regarding a safety surveillance analysis that reported a radio-opaque appearance on abdominal x-rays in patients receiving concurrent lanthanum carbonate treatment.

NDA 21-468/S-004 provides for final printed labeling for the new formulation of FOSRENOL®.

We have reviewed the final printed labeling (NDA 21-468/S-004) that you submitted in accordance with our November 23, 2005 letter, and we find it acceptable.

We have completed our review of NDA 21-468/S-005, as amended, and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

NDA 21-468/S-004
NDA 21-468/S-005

1. Under the **PRECAUTIONS** section,

a. a new subsection, **Diagnostic Tests** was added after the **General**, but before the **Long-term Effects** subsections to read:

Diagnostic Tests:
Abdominal x-rays of patients taking lanthanum carbonate may have a radio-opaque appearance typical of an imaging agent.

b. in the **Information for the Patient** subsection, a new paragraph was added:

Notify your physician that you are taking FOSRENOL® prior to an abdominal x-ray (see **PRECAUTIONS, Diagnostic Tests**).

NDA 21-468/S-004

1. In the **HOW SUPPLIED** section, the replacement of the 250 and 500 mg, old formulation, which is being depleted for the new formulation and addition of the newly approved 750 and 1000 mg formulations were added to read:

250 mg supplied in bottles of 90 tablets
NDC 54092-251-90

500 mg Patient Pack (2 bottles of 45 tablets, NDC 54092-252-45, per each patient pack)
NDC 54092-252-90

750 mg Patient Pack (6 bottles of 15 tablets, NDC 54092-253-15, per each patient pack)
NDC 54092-253-90

1000 mg Patient Pack (9 bottles of 10 tablets, NDA 54092-254-10, per each patient pack)
NDC 54092-254-90

NDA 21-468/S-005

1. In the **HOW SUPPLIED** section, the revision of the 500 mg tablet and addition of the 750 mg and 1000 mg formulations were added to read:

250 mg supplied in bottles of 400 tablets
NDC 54092-251-04

500 mg Patient Pack (2 bottles of 45 tablets, NDC 54092-252-45, per each patient pack)
NDC 54092-252-90

750 mg Patient Pack (6 bottles of 15 tablets, NDC 54092-253-15, per each patient pack)
NDC 54092-253-90

1000 mg Patient Pack (9 bottles of 10 tablets, NDA 54092-254-10, per each patient pack)
NDC 54092-254-90

As reflected in your December 9, 2005 submission, you acknowledge that for the 250 mg strength, you will be replacing the commercial bottle from a 625 cc/400 count to a 200 cc/ 90 count configuration and that you intend, once the old formulation of the 250 mg strength is depleted to manufacture only

the new formulations of FOSRENOL®. In accordance with the FDA guidance "Changes to an Approved NDA or ANDA—April 2004," the above change to the labeling (NDA 21-468/S-005) regarding the 250 mg bottle may be reported to the FDA as an annual report. You should provide stability data from the first production batch for this change in the 2005-2006 NDA annual report and annual batches thereafter on long-term stability studies.

The final printed labeling (FPL) for NDA 21-468/S-005 must be identical to the package insert submitted for NDA 21-468/S-004 that reflects all approved strengths of the new formulation. These revisions are terms for the approval of this application.

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 supplement NDA 21-468/S-005**." Approval of this submission by FDA is not required before the labeling is used.

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 this division and two copies of both 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

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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

If you have any questions, please call:

Dianne Paraoan
Regulatory Health Project Manager
(301) 796-1129

Sincerely,

{See appended electronic signature page}

Norman Stockbridge
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

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

/s/

Norman Stockbridge

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