21-468_ ORIGINAL APPROVAL_ PKG

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

21-468

Trade Name:	Fosrenol Chewable Tablets, 250- and 500 mg
Generic Name(s):	(lanthanum carbonate)
Sponsor:	Shire Pharmaceutical Development, Inc.
Agent:	
Approval Date:	October 26, 2004

Indication: Provides for use to reduce serum phosphate in patients with end stage renal disease

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Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-468

Shire Pharmaceutical Development Inc.
Attention: Lisa Wittmer, Ph.D.
1801 Research Boulevard, Suite 600
Rockville, MD 20850

Dear Dr. Wittmer:

Please refer to your new drug application (NDA) dated April 30, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for FOSRENOL (lanthanum carbonate) 250 and 500 mg Chewable Tablets.

We acknowledge receipt of your submissions dated March 31, April 11 and 24, May 2 (two), August 27 (two), September 5, and November 25, 2003, January 26, February 2, March 22, April 1 (two), May 5, 6, and 28, June 1, July 8, 12 (two), 23 and 26, August 6, 11, and 18, September 1, 7, and 10, and October 11, 14, and 20, 2004.

Your January 26, 2004 submission constituted a complete response to our February 28, 2004 approvable letter.

This new drug application provides for the use of FOSRENOL (lanthanum carbonate) Chewable Tablets to reduce serum phosphate in patients with end stage renal disease.

We have 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 submitted labeling (package insert and immediate container and carton labels submitted October 15, 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 21-468**." Approval of this submission by FDA is not required before the labeling is used.

The recommended dissolution test and method are as follows: USP apparatus 2 at a paddle speed of (b)(4) rpm in (b)(4) , with a Q of (b)(4) in 45 minutes.

An expiration date of 24 months is granted for FOSRENOL 250 and 500 mg Chewable Tablets when stored at 25°C (77°F) with excursion permitted to 15-30°C (59-86°F).

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

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 this application.

We remind you of your postmarketing study commitment to follow patients from the long-term open-label extension study (SPD405-309) for bone-related adverse events for 5 years, including patients still on lanthanum and, to the extent possible, those who have discontinued lanthanum.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol**", "**Postmarketing Study Final Report**", or "**Postmarketing Study Correspondence**."

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 Cardio-Renal 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

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, please call Ms. Denise M. Hinton, Regulatory Project Manager at (301) 594-5333

Sincerely,

{See appended electronic signature page}
Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure (Labeling)

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

/s/

Robert Temple
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