CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-687

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-687

MSP Singapore Company, LLC
Attention: Diane Louie, M.D., M.P.H.
Director, Regulatory Affairs
P.O. Box 2000, RY 32-605
Rahway, NJ 07065

Dear Dr. Louie:

Please refer to your new drug application (NDA) dated and received on September 24, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vytorin (ezetimibe/simvastatin) 10/10, 10/20, 10/40 and 10/80 mg tablets.

We acknowledge receipt of your submissions dated November 6 and 13(2), 2003, and January 22 and 23, February 12 and 17, April 13, 20, and 23, May 26, June 3, and July 13, 14 and 21, 2004.

This new drug application provides for the use of Vytorin for the following indications:

> as adjunctive therapy to diet, to reduce elevated total-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hypercholesterolemia or mixed hyperlipidemia and
>
> for the reduction of elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia, as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or alone, if such treatments are unavailable.

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

The final printed labeling (FPL) must be identical to the package insert (submitted July 14, 2004), patient package insert (submitted July 13, 2004) and the following enclosed carton and container labels:

Label type	**Strength**	**Count**	**Date Submitted**
Bottle	10/10; 10/20; 10/40; 10/80	90-ct	September 24, 2003
Bottle	10/40; 10/80	500-ct	September 24, 2003
Bottle	10/10; 10/20	1000-ct	September 24, 2003
Bottle	10/10; 10/20; 10/40; 10/80	30-ct	May 26, 2004
Blister	10/10; 10/20; 10/40; 10/80	Unit dose	May 26, 2004
Carton	10/10; 10/20	100-ct unit dose	May 26, 2004
Carton	10/40; 10/80	50-ct unit dose	July 21, 2004 (not enclosed)

Marketing the products with FPL that is not identical to the approved labeling text may render the products 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-NDAs*. Alternatively, you may submit 20 paper copies of 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 21-687."** 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 children < 10 years of age for all indications and for children aged 10 to 17 years for homozygous familial hypercholesterolemia. We are deferring the pediatric study requirement for children 10 years to < 18 years of age for the treatment (adjunctive to diet) of patients with primary hypercholesterolemia or mixed dyslipidemia 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 status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment (adjunctive to diet) of primary hypercholesterolemia or mixed dyslipidemia in pediatric patients age 10 years to < 18 years of age.

Final Report Submission: July 31, 2009.

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

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 and patient 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).

If you have any questions, call Monika Johnson, Regulatory Project Manager, at (301) 301-827-9087.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug
Products, HFD-510
Office of Drug Evaluation II
Center of Drug Evaluation and Research

Enclosures: Package Insert
Patient Package Insert
Carton and Container Labels

APPEARS THIS WAY
ON ORIGINAL

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

/s/

David Orloff
7/23/04 05:50:04 PM

APPEARS THIS WAY
ON ORIGINAL