



NDA 21445/S-030

**SUPPLEMENT APPROVAL**

MSP Singapore Company, LLC  
Attention: Jeffrey R. Tucker, M.D., Agent  
Senior Director, Regulatory Affairs  
P.O. Box 1000, UG2CD-48  
North Wales, PA 19454-1099

Dear Dr. Tucker:

Please refer to your Supplemental New Drug Application (sNDA) dated September 30, 2010, received September 30, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zetia (ezetimibe) 10 mg Tablets.

We acknowledge receipt of your amendments dated November 1, 2010, and January 13, June 24, July 14, 22, and 27, 2011.

This "Prior Approval" supplemental new drug application provides for the inclusion of the lipid parameter non-HDL-C in the **INDICATIONS AND USAGE**, Primary Hyperlipidemia indication and in the **CLINICAL PHARMACOLOGY**, Pharmacodynamics and **CLINICAL STUDIES**, Primary Hyperlipidemia sections of the Zetia package insert. Additional information has been added to the **OVERDOSAGE** section of the label.

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

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert and for the patient package insert), with the addition of any labeling changes in pending "Changes Being Effectuated" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

<http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to nine years because the number of pediatric patients who would be appropriate for treatment with lipid-lowering agents is small and this would make the studies impossible or highly impractical to complete.

We are deferring submission of your pediatric study for ages 10 to 17 years for this application because pediatric studies should be delayed until additional safety or effectiveness data have been collected.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

1806-1      Pediatric Plan in Adolescents at High Risk for Cardiovascular Disease with Primary Hypercholesterolemia

Final Protocol Submission:    March 31, 2012  
Study/Trial Completion:        June 30, 2019  
Final Report Submission:        December 31, 2019

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED**

**PEDIATRIC ASSESSMENTS"** in large font, bolded type at the beginning of the cover letter of the submission.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **REPORTING REQUIREMENTS**

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 Margaret Simoneau, M.S., RPh., Regulatory Project Manager, at (301) 796-1295.

Sincerely,

*{See appended electronic signature page}*

Eric Colman, M.D.  
Deputy Director  
Division of Metabolism and Endocrinology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

ENCLOSURE:

Content of Labeling

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

/s/  
-----

ERIC C COLMAN  
07/29/2011