DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20632/S-034 and S-035

SUPPLEMENT APPROVAL

Abbott Laboratories
Attention: Natalie Tolli, B.Pharm, M.S.
Director, Global Pharmaceutical Regulatory Affairs
Dept. PA76, Bldg. AP30-1NE
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Tolli:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received January 29 (S-034), and April 7, 2010 (S-035), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for MERIDIA (sibutramine hydrochloride) Capsules, 5 mg, 10 mg, and 15 mg.

We acknowledge receipt of your amendments dated July 16, 2010 (to supplement -035) and July 30, 2010 (to supplement -034).

Supplement -034, dated January 29, 2010, is a "Changes Being Effected" supplemental new drug application that provides for the following revisions to the package insert:

To the **CLINICAL PHARMACOLOGY** section, Special Population, Geriatric subsection, at the end of the paragraph, the addition of:

- Sibutramine is contraindicated in patients over 65 years of age (see **CONTRAINDICATIONS**).

The **CONTRAINDICATIONS** section has been revised to read as follows:

MERIDIA is contraindicated in patients:

- with a history of coronary artery disease (e.g., angina, history of myocardial infarction), congestive heart failure, tachycardia, peripheral arterial occlusive disease, arrhythmia or cerebrovascular disease (stroke or transient ischemic attack (TIA)) (see **WARNINGS**).
- with inadequately controlled hypertension > 145/90 mm Hg (see **WARNINGS**).
- over 65 years of age.
- receiving monoamine oxidase inhibitors (MAOIs) (see **WARNINGS**).

- with hypersensitivity to sibutramine or any of the inactive ingredients of MERIDIA.
- who have a major eating disorder (anorexia nervosa or bulimia nervosa).
- taking other centrally acting weight loss drugs.

To the **WARNINGS** section, a modification of the following subsection, and its relocation to the top of the section so it now reads:

Concomitant Cardiovascular Disease

- Due to an increased risk of heart attack and stroke in patients with cardiovascular disease, MERIDIA should not be used in patients with a history of coronary artery disease, congestive heart failure, arrhythmias, or stroke.

To the **PRECAUTIONS** section, Geriatric Use subsection, a modification of the paragraph to read:

- Clinical studies of sibutramine did not include sufficient numbers of patients over 65 years of age. Sibutramine is contraindicated in this group of patients (see **CONTRAINDICATIONS**). Pharmacokinetics in elderly patients are discussed in "**CLINICAL PHARMACOLOGY**."

Supplement -035, dated April 7, 2010, is a Prior Approval supplemental drug application providing for the conversion of the approved patient package insert to a Medication Guide, revisions to the container labels, and your proposed risk evaluation and mitigation strategy (REMS).

We have completed our review of these applications, as amended. These applications are **approved**, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). The details of the REMS requirements were outlined in our REMS notification letter dated March 9, 2010.

Since MERIDIA (sibutramine hydrochloride) was approved on November 22, 1997, we have become aware of new clinical trial data from the Sibutramine Cardiovascular Outcomes Trial (SCOUT), showing an increased risk of major adverse cardiovascular events in patients with a history of cardiovascular disease using MERIDIA (sibutramine hydrochloride). We considered this information to be “new safety information” as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on April 7, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide included with this letter and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to an evaluation of patients' understanding of the serious risks of MERIDIA (sibutramine hydrochloride).

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 20632 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 20632
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 20632
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert and text for the Medication Guide) 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.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (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.

IMMEDIATE CONTAINER LABELS

Submit final printed container labels that are identical to the enclosed container labels (submitted on April 7, 2010) as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Container Labels for approved NDA 20632/S-035**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in these supplements including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 Patricia Madara, Regulatory Project Manager, at (301) 796-1249.

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

Enclosures:
- Content of Labeling
- Container Labeling
- REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20632	SUPPL-35	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	MERIDIA (SIBUTRAMINE HCL MONOHYDRATE)
NDA-20632	SUPPL-34	ABBOTT LABORATORIES PHARMACEUTICAL PRODUCTS DIV	MERIDIA (SIBUTRAMINE HCL MONOHYDRATE)

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
08/04/2010