



NDA 018074/S-034

**SUPPLEMENT APPROVAL**

Sandoz, Inc.  
Attention: Bernadette Attinger  
Director, Regulatory Affairs  
506 Carnegie Center; Suite 400  
Princeton, NJ 08540

Dear Ms. Attinger:

Please refer to your Supplemental New Drug Application (sNDA) dated October 19, 2011, received October 20, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for phendimetrazine tartrate SR capsules, 105 mg.

We acknowledge receipt of your email dated January 30, 2012, stating your agreement to the labeling revisions that we communicated to you by email on January 23, 2012.

This "Prior Approval" supplemental new drug application, submitted in response to our supplement request letter dated September 20, 2011, provides for the following labeling changes:

1. Addition of "**Pregnancy**" to the **CONTRAINDICATIONS** section and revision of the **Pregnancy Category** from "**C**" to "**X**."
2. Addition of "**Nursing**" to the **CONTRAINDICATIONS** section and revision of the "**Nursing Mothers**" subsection of the **PRECAUTIONS** section.
3. Revision of the **CONTRAINDICATIONS** section to include "history of cardiovascular disease" and add "stroke," "arrhythmias," and "congestive heart disease."
4. Deletion of the "**Usage in Pregnancy**" subsection in the **PRECAUTIONS** section.
5. Revision of the "**Pediatric Use**" subsection of the **PRECAUTIONS** section to include the following language: "Because pediatric obesity is a chronic condition requiring long-term treatment, the use of phendimetrazine tartarate ER approved for short-term therapy, is not recommended in patients less than 17 years of age."
6. Addition of "**Renal Impairment**" and "**Geriatric Use**" subsections to the **PRECAUTIONS** section.

7. Deletion of the following sentences from the **WARNINGS** section: “To limit unwarranted exposure and risks, treatment with phendimetrazine tartrate should be continued only if the patient has satisfactory weight loss within the first 4 weeks of treatment (i.e., weight loss of at least 4 pounds, or as determined by the physician and patient).”
8. Revision of the “**Drug Interactions**” subsection of the **PRECAUTIONS** section to include the following possible drug interactions:
  - “Monoamine Oxidase Inhibitors  
Use of phendimetrazine tartrate is contraindicated during or within 14 days following the administration of monoamine oxidase inhibitors because of the risk of hypertensive crisis.
  - Alcohol  
Concomitant use of alcohol with phendimetrazine tartrate may result in an adverse drug reaction.
  - Insulin and Oral Hypoglycemic Medications  
Requirements may be altered.
  - Adrenergic Neuron Blocking Drugs  
phendimetrazine tartrate may decrease the hypotensive effect of adrenergic neuron blocking drugs.”
9. Revision of the “**Drug Interactions**” subsection of the **PRECAUTIONS** section to delete the following sentence: “Efficacy of phendimetrazine tartrate with other anorectic agents has not been studied and the combined use may have the potential for serious cardiac problems.”
10. Revision of the **ADVERSE EVENTS** section to add the following information:
  - ”The following adverse reactions are described, or described in greater detail, in other sections:
    - Primary pulmonary hypertension (see *Warnings*)
    - Valvular heart disease (see *Warnings*)
    - Effect on the ability to engage in potentially hazardous tasks (see *Warnings*)
    - Withdrawal effects following prolonged high dosage administration (see *Drug Abuse and Dependence*)”
11. Revision of the “**Cardiovascular**” subsection of the **ADVERSE EVENTS** section to add “Primary pulmonary hypertension, and/or regurgitant cardiac valvular disease, palpitation, tachycardia, elevated blood pressure, and ischemic events”, and delete the following statements: “Valvular heart disease associated with the use of some anorectic agents such as fenfluramine and dexfenfluramine, both independently and especially when used in combination with other anorectic drugs, has been reported. However, no case of this valvulopathy has been reported when phendimetrazine tartrate has been used alone.”

12. Addition of an “**Abuse**” subsection to the **DRUG ABUSE AND DEPENDENCE** section and inclusion of the following statements which were transferred from the “**Dependence**” subsection: “Phendimetrazine tartrate is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of phendimetrazine should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program.”
13. Addition of a “**Chronic Intoxication**” subsection to the **OVERDOSAGE** section and inclusion of the following statements: “Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia. (See *Drug Abuse and Dependence*)”

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

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), 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).

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  
Office of Prescription Drug Promotion (OPDP)  
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 Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

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

ENCLOSURE:  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ERIC C COLMAN  
02/10/2012