



NDA 018948/S-026  
NDA 019257/S-012  
NDA 020182/S-013

**SUPPLEMENT APPROVAL**

Sigma-Tau Pharmaceuticals, Inc.  
Attention: Gianfranco Fornasini, Ph.D.  
Senior Vice President, Scientific Affairs  
9841 Washingtonian Boulevard, Suite 500  
Gaithersburg, MD 20878

Dear Dr. Fornasini:

Please refer to your Supplemental New Drug Applications (sNDAs) dated October 17, 2013, received October 18, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for:

<u>NDA</u>	<u>Supplement</u>	<u>Drug Product</u>
018948	S-026	Carnitor (levocarnitine) Tablets, 330 mg
019257	S-012	Carnitor (levocarnitine) Oral Solution, 100 mg/mL Carnitor SF (levocarnitine) Sugar-Free Oral Solution, 100 mg/mL
020182	S-013	Carnitor (levocarnitine) Injection, 200 mg/mL

These “Prior Approval” supplemental new drug applications provide for the addition of a Drug Interactions subsection to the Precautions section of the package inserts. Other minor editorial revisions have also been proposed.

We also refer to your agreement with our revisions to the package inserts via email to Jennifer Johnson of this Division on May 6, 2015.

**APPROVAL & LABELING**

We have completed our review of these supplemental applications, as amended. They are 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), 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 that includes labeling changes 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.

Because none of these criteria apply to your application, you are exempt from this requirement.

### **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  
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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. 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>.

### **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, please call Jennifer Johnson, Regulatory Health Project Manager, at (301) 796-2194.

Sincerely,

*{See appended electronic signature page}*

Jean-Marc Guettier, M.D.  
Director  
Division of Metabolism and Endocrinology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

ENCLOSURES:      Package Inserts for:

1. Carnitor (levocarnitine) Tablets, Carnitor (levocarnitine) Oral Solution and Carnitor SF (levocarnitine) Sugar-Free Oral Solution
2. Carnitor (levocarnitine) Injection

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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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JEAN-MARC P GUETTIER  
05/29/2015