



NDA 18012/S-031  
NDA 18013/S-063  
NDA 17090/S-078  
NDA 19906/S-039

## SUPPLEMENT APPROVAL

Mallinckrodt Inc.  
Attention: Linda F. Noa  
Senior Manager, Regulatory Strategy  
675 McDonnell Boulevard (30-2)  
Hazelwood, MO 63042

Dear Ms. Noa:

Please refer to your Supplemental New Drug Applications (sNDA) dated July 17, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pamelor (nortriptyline HCl) 10 mg/5 ml Solution (NDA 18012), Pamelor (nortriptyline HCl) 10 mg, 25 mg, 50 mg, and 75mg Capsules (NDA 18013), Tofranil-PM (imipramine pamoate) 75 mg, 100 mg, 125 mg, and 150 mg Capsules (NDA 17090), and Anafranil (clomipramine) 25 mg, 50 mg, and 75 mg Capsules (NDA 19906).

These "Changes Being Effected" supplemental new drug applications provide for the addition of a new subsection under **Adverse Reactions** entitled Postmarketing Experience.

### **APPROVAL & LABELING**

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

We note that your July 17, 2014, submission includes final printed labeling (FPL) for your package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

### **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 Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (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).

### **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, email CDR Renmeet Grewal, Pharm.D., Senior Regulatory Project Manager, at [Renmeet.Grewal@fda.hhs.gov](mailto:Renmeet.Grewal@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Mitchell V. Mathis, M.D.  
CAPT, USPHS  
Director  
Division of Psychiatry Products  
Office of Drug Evaluation I  
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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MITCHELL V Mathis  
07/28/2014