



NDA 19906/S-037  
NDA 18012/S-029  
NDA 18013/S-061  
NDA 17090/S-076

## SUPPLEMENT APPROVAL

Mallinckrodt Inc.  
Attention: Linda Noa  
Senior Manager, Regulatory Strategy  
675 McDonnell Blvd.  
Hazelwood, MO 63042

Dear Ms. Noa:

Please refer to your Supplemental New Drug Applications (sNDA) dated May 4 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Anafranil (clomipramine) 25 mg, 50 mg, and 75 mg Capsules (NDA 19906), Pamelor (nortriptyline HCl) 10 mg/5 ml Solution (NDA 18012), Pamelor (nortriptyline HCl) 10 mg, 25 mg, 50 mg, and 75 mg Capsules (NDA 18013), and Tofranil-PM (imipramine pamoate) 75 mg, 100 mg, 125 mg, and 150 mg Capsules (NDA 17090).

We acknowledge receipt of your amendments dated July 27, 2012, and September 24, 2012.

These "Prior Approval" supplemental new drug applications provide for class labeling revisions to the **Contraindications, Warnings, Dosage And Administration, & Medication Guide** regarding serotonin toxicity associated with the co-administration of linezolid and methylene blue as requested in an Agency supplement request letter dated March 5, 2012.

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 and with the minor editorial revisions agreed upon in an email communication dated October 23, 2012, between you and Paul David, of this Agency.

### **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, except with the revisions agreed upon in the September 24, 2012

communication, 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}*

Thomas Laughren, M.D.  
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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THOMAS P LAUGHREN  
10/26/2012