



NDA 17-812 / S-023

NDA 18-421 / S-021

Roxane Laboratories, Inc.
Attn: Ms. Ann Malony
P.O. Box 16532
Columbus, Ohio 43216

Dear Ms. Malony:

Please refer to your supplemental new drug applications referenced above, dated August 29, 2002 and received August 30, 2002, which were submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lithium Carbonate Capsules and Lithium Citrate Syrup.

These “Changes Being Effected” supplements provide for revisions to the package insert in response to an Agency letter dated February 4, 2002, which is incorporated into this letter by reference. The February 4, 2002 letter requested your firm to revise the labeling for these products to include standardized language specifically mentioning the need for close monitoring of lithium levels in patients taking COX-2 inhibitors and lithium.

We have completed our review of these supplemental new drug applications. They are approved, effective on the date of this letter.

However, in the course of our review we have identified some inconsistencies in both the package insert and the related container labeling for these drug products. We are therefore requesting that you revise your labeling for these products at the next printing to incorporate the following changes, which will furnish more adequate information on the safe and effective use of these drug products:

1. Requested changes to the Package Insert

- **PRECAUTIONS: Drug Interactions.** Please delete the paragraph in this section of the package insert that begins with “Indomethacin and piroxicam...” and concludes with “...increased plasma lithium level monitoring is recommended.” The paragraph added to this section in accordance with our February 4, 2002 letter addresses the same issue, using standardized language.

- **HOW SUPPLIED.** Please replace the current storage statement with the following text:

Store and Dispense:

Lithium Carbonate Capsules: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Protect from moisture. Dispense in a tight container as defined in the USP/NF.

Lithium Citrate Syrup: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Dispense in a tight container as defined in the USP/NF. This text represents our recommended storage conditions, and utilizes the standard “Controlled Room Temperature Storage” language recommended by the USP.

2. Requested Changes to the Container Labeling for Both Drug Products (All Packaging Configurations)

- Please revise the controlled room temperature storage statement on this labeling to correspond to USP recommended language (see above).
- A shorter version of the USP recommended language reads as follows: “Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).” This shorter statement may be used on the container labeling where limited space is available.
- No other changes are requested with respect to the product- and package-specific storage instructions already present on the container labeling.

The revised package insert and container labeling should be submitted *en bloc* to the next Annual Report following their printing, for both NDAs. To facilitate review, please provide a highlighted or marked-up copy of labeling that shows the changes that have been made.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81. Please note that, if you elect to make any additional changes beyond those provided for in this letter, the labeling may need to be submitted *en bloc* as either a “Changes Being Effected” supplement or a Prior Approval supplement, depending on the nature of the additional changes made.

If you have any questions, please call Doris J. Bates, Ph.D., Regulatory Project Manager, at (301) 594-2850.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Russell Katz

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