DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug
Administration
Rockville MD 20857

NDA 16-860/S-059, S-065, S-067, S-068, S-069, S-072
NDA 18-152/S-003, S-008, S-010, S-012, S-013, S-016

SmithKline Beecham Corporation
d/b/a GlaxoSmithKline
Attention: Elizabeth McConnell, Pharm.D.
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Dr. McConnell:

Please refer to the following supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lithium Carbonate Capsules and Lithium Carbonate Controlled Release Tablets.

16-860/SLR-059 (dated October 8, 1984)
18-152/SLR-003

These "Changes Being Effected" supplements provide for revisions to the ADVERSE REACTIONS:Cardiovascular subsection of the package insert to include sinus node dysfunction with severe bradycardia (which may result in syncope).

16-860/SLR-065 (dated February 11, 1988)
18-152/SLR-008

These "Changes Being Effected" supplements provide for revisions the PRECAUTIONS section of labeling to describe a drug interaction with metronidazole.

16-860/SLR-067 (dated February 14, 1992)
18-152/SLR-010

These "Changes Being Effected" supplements provide for revisions to the package insert in response to an Agency letter dated July 11, 1991, which requested all lithium NDA holders to revise their labeling

to expand the existing description of the drug interaction that occurs when lithium and diuretics or angiotensin converting enzyme (ACE) inhibitors are used concomitantly.

16-860/SLR-068 (dated August 15, 1995)
18-152/SLR-012

These "Changes Being Effected" supplements provide for revisions to the ADVERSE REACTIONS:Miscellaneous subsection of the package insert to add the term myasthenia gravis and other minor editorial changes.

16-860/SLR-069 (dated February 26, 1997)
18-152/SLR-013

These "Changes Being Effected" supplements provide for revisions to the PRECAUTIONS section of the package insert to include language regarding drug interactions between lithium and selective serotonin reuptake inhibitors (SSRIs), methyldopa, phenytoin, and carbamazepine.

16-860/SLR-072 (dated February 21, 2000)
18-152/SLR-016

These "Changes Being Effected" supplements provide for revisions to the DESCRIPTION and HOW SUPPLIED sections of the package insert to reflect changes resulting from a transfer of manufacturing site (S-070 provided for this transfer of manufacturing site and was approved on February 1, 2000).

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted February 21, 2000). Accordingly, these supplemental applications are approved effective on the date of this letter.

We additionally request, at the next printing of your labels and labeling, that you replace the presently used storage recommendations statement under the HOW SUPPLIED section of the package insert as well as the container labels with the following statement:

> "Store at 25°C (77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]".

This change may be reported in your next annual report.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Doris Bates, Ph.D., Regulatory Management Officer, 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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