DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 018817/S-024

SUPPLEMENT APPROVAL

G.D. Searle LLC
c/o Pfizer Inc.
Attention: Michele Burtness
Manager, Regulatory Affairs
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Burtness:

Please refer to your Supplemental New Drug Application (sNDA) dated December 29, 2010 received December 29, 2010 submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Calan (verapamil hydrochloride) 80 mg and 120 mg Tablets.

This "Changes Being Effected" supplemental new drug application provides for changes to the **PRECAUTIONS** and **ADVERSE REACTIONS** section of the package insert.

1. Under **PRECAUTIONS**, the following was added:

   In the section – **Use in patients with attenuated (decreased) neuromuscular transmission:** "and causes a worsening of myasthenia gravis" was added.

2. Under **PRECAUTIONS**, the following was added:

   Drug Interactions:
   Cytochrome inducers/inhibitors: *In vitro* metabolic studies indicate that verapamil is metabolized by cytochrome P450 CYP3A4, CYP1A2, CYP2C8, CYP2C9 and CYP2C18. Clinically significant interactions have been reported with inhibitors of CYP3A4 (e.g., erythromycin, ritonavir) causing elevation of plasma levels of verapamil while inducers of CYP3A4 (e.g., rifampin) have caused a lowering of plasma levels of verapamil.

   Aspirin: In a few reported cases, co-administration of verapamil with aspirin has led to increased bleeding times greater than observed with aspirin alone.

   Grapefruit juice: Grapefruit juice may increase plasma levels of verapamil.

3. Under **ADVERSE REACTIONS**, the following was added:

   In the sub-section *Nervous system: "extrapyramidal symptoms"* was added.

We have completed our review of this supplemental application. It is 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, text for the patient package insert), 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, please call Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

{See appended electronic signature page}
Mary Ross Southworth, PharmD
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

/s/

MARY R SOUTHWORTH
06/29/2011