DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020092/S-017

SUPPLEMENT APPROVAL

Watson Laboratories, Inc.
Attention: Wendy DeSpain, BS, MBA, RAC
Associate Director, Regulatory
577 Chipeta Way
Salt Lake City, UT 84108

Dear Ms. DeSpain:

Please refer to your Supplemental New Drug Application (sNDA) dated March 21, 2011, and received March 22, 2011, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dilacor XR (diltiazem hydrochloride) 120 mg, 180 mg, and 240 mg Extended Release Capsules.

This "Changes Being Effected" supplemental new drug application provides for labeling revised as follows:

1. Under **PRECAUTIONS, Drug Interactions**, the following section was changed from:

(b) (4)

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To:

Statins: Diltiazem is an inhibitor of CYP3A4 and has been shown to increase significantly the AUC of some statins. The risk of myopathy and rhabdomyolysis with statins metabolized by CYP3A4 may be increased with concomitant use of diltiazem. When possible, use a non-CYP3A4-metabolized statin with diltiazem; otherwise, dose adjustments for both diltiazem and the statin should be considered along with close monitoring for signs and symptoms of any statin related adverse events.

In a healthy volunteer cross-over study (N=10), co-administration of a single 20 mg dose of simvastatin at the end of a 14 day regimen with 120 mg twice daily diltiazem SR resulted in a 5-fold higher mean simvastatin AUC compared with simvastatin alone. High average steady-state exposures of diltiazem would result in a greater increase in simvastatin exposure. A daily dose of 480 mg of diltiazem would be expected to result in an 8-fold higher mean simvastatin AUC compared with simvastatin alone. If coadministration of simvastatin with diltiazem is required, limit the daily doses of simvastatin to 10 mg and diltiazem to 240 mg.

In a ten-subject randomized, open label, 4-way cross-over study, co-administration of diltiazem (120 mg twice daily diltiazem SR for 2 weeks) with a single 20 mg dose of lovastatin resulted in 3- to 4-fold higher mean lovastatin AUC and Cmax values compared with lovastatin alone. In the same study, there was no significant change in 20 mg single dose pravastatin AUC and Cmax during diltiazem coadministration.

2. The revision date and version number were updated.

We have completed our review of this supplemental application, and 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), 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:

Lori Anne Wachter, RN, BSN
Regulatory Project Manager for Safety
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

ENCLOSURE:
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
06/07/2011